IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

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Sankyo Company, Limited
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SANKYO COMPANY, LIMITED, and DAIICHI SANKYO, INC.	:	Civil Action No. _____
Plaintiffs,	:	COMPLAINT FOR PATENT INFRINGEMENT AND CERTIFICATION PURSUANT TO LOCAL CIVIL RULE 11.2
v.	:	
MYLAN PHARMACEUTICALS, INC. and MYLAN LABORATORIES, INC.,	:	JURY TRIAL DEMANDED
Defendants.	:	

Plaintiffs Sankyo Company, Limited and Daiichi Sankyo, Inc. (hereinafter "Plaintiffs"), for their Complaint against Defendants Mylan Pharmaceuticals, Inc. and Mylan Laboratories, Inc., allege as follows:

NATURE OF ACTION

1. This is an action for patent infringement.

PARTIES

2. Plaintiff Sankyo Company, Limited ("Sankyo Japan") is a corporation organized and existing under the laws of Japan, having a place of business at 5-1, Nihonbashi Honcho 3-chome, Chuo-ku, Tokyo 103-8426, Japan.

3. Plaintiff Daiichi Sankyo, Inc. ("Sankyo U.S.") is a corporation organized and existing under the laws of the State of Delaware, having a principal place of business at Two Hilton Court, Parsippany, New Jersey 07054.

4. On information and belief, Mylan Pharmaceuticals, Inc. ("Mylan Pharmaceuticals") is a corporation organized under the laws of the State of West Virginia, having an office and place of business at 781 Chestnut Ridge Road, Morgantown, West Virginia 26505.

5. On information and belief, Mylan Laboratories, Inc. ("Mylan Laboratories") is a corporation organized under the laws of the State of Pennsylvania, having an office and place of business at 1500 Corporate Drive, Canonsburg, Pennsylvania 15317.

6. On information and belief, Mylan Pharmaceuticals is a wholly-owned subsidiary of Mylan Laboratories, and the acts of Mylan Pharmaceuticals complained of herein were aided and abetted by and done with the cooperation, participation, and assistance of Mylan Laboratories. On information and belief, Mylan Pharmaceuticals and Mylan Laboratories have officers or directors in common.

7. Mylan Pharmaceuticals and Mylan Laboratories are hereinafter collectively referred to as "Mylan."

JURISDICTION AND VENUE

8. This action arises under the patent laws of the United States of America. This Court has jurisdiction over the subject matter of this action under 28 U.S.C. §§ 1331 and 1338(a).

9. On information and belief, Mylan Pharmaceuticals is registered to do business in New Jersey and has a registered agent in New Jersey. In addition, Mylan sells various products and does business throughout the United States, including within this judicial district. Upon information and belief, Mylan has submitted to the jurisdiction of the United States District Court for the District of New Jersey. This Court has personal jurisdiction over Mylan by virtue of, *inter alia*, the above-mentioned facts.

10. Venue is proper in this Court pursuant to 28 U.S.C. §§ 1391(b) and (c), and 28 U.S.C. § 1400(b).

CLAIM FOR RELIEF - PATENT INFRINGEMENT

11. Plaintiff Sankyo U.S. holds an approved new drug application ("NDA") No. 21-286 for Benicar® tablets (5 mg, 20 mg and 40 mg), which tablets contain the active ingredient Olmesartan Medoxomil. Benicar® tablets were approved by the United States Food and Drug Administration ("FDA") on April 25, 2002, for treatment of hypertension. Olmesartan Medoxomil is an angiotensin II receptor antagonist.

12. Sankyo Japan is the owner of United States Letters Patent No. 5,616,599 ("the '599 patent"). The '599 patent was duly and legally issued on April 1, 1997. A true copy of the '599 patent is attached hereto as Exhibit A.

13. The '599 patent claims various chemical compounds including Olmesartan Medoxomil specifically, as well as pharmaceutical compositions containing these compounds, and method for the treatment or prophylaxis of hypertension administering these compounds.

14. The '599 patent was assigned by the inventors to Sankyo Japan and remains assigned to Sankyo Japan.

15. Sankyo U.S. is a licensee under the '599 patent and is marketing and selling in the United States the Benicar® tablets manufactured by Sankyo Japan.

16. Mylan Pharmaceuticals submitted to the FDA an abbreviated new drug application ("ANDA") under the provisions of 21 U.S.C. § 355(j), seeking approval to engage in the commercial manufacture, use, offer for sale, sale and/or importation of generic Olmesartan Medoxomil tablets 5 mg, 20 mg and 40 mg (hereinafter referred to as "Mylan's ANDA Product").

17. Mylan submitted its ANDA to the FDA for the purpose of obtaining approval to engage in the commercial manufacture, use, offer for sale, sale and/or importation of Mylan's ANDA Product before the expiration of the '599 patent.

18. By filing the ANDA under 21 U.S.C. § 355(j) for the purpose of obtaining approval to engage in the commercial manufacture, use, offer for sale, sale and/or importation of Mylan's ANDA Product before the expiration of the '599 patent, Mylan has committed an act of infringement under 35 U.S.C. § 271(e)(2). Further, the commercial manufacture, use, offer for sale, sale and/or importation of Mylan's ANDA Product for which Mylan seeks approval in its ANDA will also infringe one or more claims of the '599 patent.

19. Mylan made, and included in its ANDA, a certification under 21 U.S.C. § 355(j)(2)(A)(vii)(IV) that, in its opinion and to the best of its knowledge, the '599 patent is invalid.

20. Plaintiffs are entitled to the relief provided by 35 U.S.C. § 271(e)(4), including an Order of this Court that the effective date of any approval of the aforementioned ANDA relating to Mylan's ANDA Product be a date which is not earlier than April 25, 2016, the expiration of the '599 patent, or any later date of exclusivity to which Plaintiffs become entitled. Further, Plaintiffs are entitled to an award of damages for any commercial manufacture, use, offer for sale, sale and/or importation of Mylan's ANDA Product, and any act committed by Mylan with respect to the subject matter claimed in the '599 patent, which act is not within the limited exclusions of 35 U.S.C. § 271(e)(1).

21. On information and belief, when Mylan filed its ANDA, it was aware of the '599 patent and that the filing of its ANDA with the request for its approval prior to the expiration of the '599 patent was an act of infringement of this patent.

22. The relevant statute (21 U.S.C. § 355(j)(2)(B)(iv)(II)) requires that a notice of the Paragraph IV certification ("Notice Letter") "include a detailed statement of the factual and legal basis of the opinion of the applicant that the patent is invalid or will not be infringed." The FDA Rules and Regulations (21

C.F.R. § 314.95(c)(6)(ii)) further require that the detailed statement include "[f]or each claim of a patent alleged to be invalid or unenforceable, a full and detailed explanation of the grounds supporting the allegation."

23. On or about June 19, 2006, Mylan sent a Notice Letter, purporting to comply with the provisions of 21 U.S.C. § 355(j)(2)(B)(iv)(II) and the FDA regulations relating thereto, to Plaintiffs. The Notice Letter, as sent by Mylan, was received by Sankyo U.S. on June 20, 2006 and by Sankyo Japan on June 21, 2006.

24. In the Notice Letter, Mylan failed to comply with the statutory provisions set forth in paragraph 22, above. The Notice Letter does not present a *prima facie* case of invalidity of the claims of the '599 patent. Mylan's Notice Letter does not allege that the '599 patent was unenforceable. Other than the allegation of invalidity, Mylan's Notice Letter does not provide an independent allegation of noninfringement. On information and belief, Mylan lacked a good faith basis for alleging invalidity when the ANDA was filed. Mylan's ANDA and certification filing is a wholly unjustified infringement of the '599 patent.

25. Mylan has violated its duty of due care to avoid the known patent right of the '599 patent.

26. This is an exceptional case and Plaintiffs are entitled to an award of reasonable attorneys fees under 35 U.S.C. § 285.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs respectfully request the following relief:

A. Judgment that Mylan has infringed one or more claims of the '599 patent by filing the aforesaid ANDA relating to Mylan's ANDA Product;

B. Judgment that manufacture, use, sale or offer for sale of Mylan's ANDA Product will infringe Sankyo Japan's '599 patent;

C. A permanent injunction restraining and enjoining Mylan and its officers, agents, attorneys and employees, and those acting in privity or concert with it, from engaging in the commercial manufacture, use, offer to sell, sale within the United States, or importation into the United States, of Mylan's ANDA Product as claimed in the '599 patent;

D. An Order that the effective date of any approval of the aforementioned ANDA relating to Mylan's ANDA Product be a date which is not earlier than the expiration of the right of exclusivity under the '599 patent, or any later date of exclusivity to which Plaintiffs become entitled;

E. Damages from Mylan for any commercial activity constituting infringement of the '599 patent;

F. Judgment that this is an exceptional case under 35 U.S.C. § 285, and Plaintiffs are entitled to the costs and reasonable attorneys fees in this action; and

G. Such other and further relief as the Court may deem just and proper.

JURY DEMAND

Pursuant to Fed. Rule Civ. P. 38 (b), Plaintiffs hereby demand trial by jury of all claims and issues triable to a jury.

CERTIFICATION PURSUANT TO L. CIV. R. 11.2

Pursuant to Local Civil Rule 11.2, I hereby certify that the within action is not the subject of any other action pending in any Court, or of any pending arbitration or administrative proceeding.

Dated: July 31, 2006

s/ William J. Heller
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EXHIBIT A

US005616599A

United States Patent [19]

Yanagisawa et al.

[11] **Patent Number: 5,616,599**

[45] **Date of Patent: Apr. 1, 1997**

[54] **ANGIOTENSIN II ANTAGOSIST 1-BIPHENYLMETHYLIMIDAZOLE COMPOUNDS AND THEIR THERAPEUTIC USE**

[75] Inventors: **Hiroaki Yanagisawa; Koichi Fujimoto; Yoshiya Amemiya; Yasuo Shimoji; Takuro Kanazaki; Hiroyuki Koike; Toshio Sada**, all of Tokyo, Japan

[73] Assignee: **Sankyo Company, Limited**, Tokyo, Japan

[21] Appl. No.: **378,650**

[22] Filed: **Jan. 26, 1995**

Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 839,482, Feb. 20, 1992, abandoned, and Ser. No. 69,595, Jun. 1, 1993, abandoned.

[30] **Foreign Application Priority Data**

Feb. 21, 1991	[JP]	Japan	3-027098
Apr. 26, 1991	[JP]	Japan	3-096588
Jun. 6, 1991	[JP]	Japan	3-134889
Jul. 8, 1991	[JP]	Japan	3-167138
Jul. 15, 1991	[JP]	Japan	3-173972
Jul. 24, 1991	[JP]	Japan	3-184841
Jun. 2, 1992	[JP]	Japan	4-141160

[51] **Int. Cl.**[6] **C07D 403/10**; C07D 257/04; A61K 31/41; A61K 31/415

[52] **U.S. Cl.** **514/381**; 514/382; 514/396; 514/397; 548/253; 548/315.1; 548/315.4; 548/334.5

[58] **Field of Search** 548/253, 315.1, 548/315.4, 334.5; 514/381, 382, 396, 397

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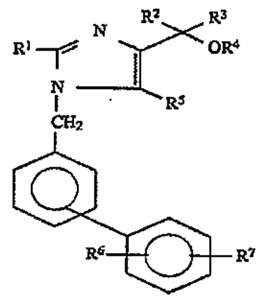
(List continued on next page.)

Primary Examiner—David B. Springer
Attorney, Agent, or Firm—Frishauf, Holtz, Goodman, Langer & Chick, P.C.

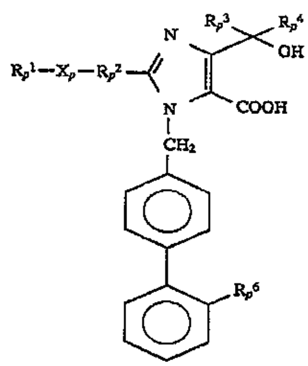
[57] **ABSTRACT**

Compounds of the following formula (I) or the formula $(I)_p$:

(I)



$(I)_p$



wherein R^1 is alkyl or alkenyl; R^2 and R^3 are hydrogen, alkyl, alkenyl, cycloalkyl, aralkyl, aryl, or aryl fused to cycloalkyl; R^4 is hydrogen, alkyl, alkanoyl, alkenoyl, arylcarbonyl, alkoxycarbonyl, tetrahydropyranyl, tetrahydrothiopyranyl, tetrahydrothienyl, tetrahydrofuryl, a group of formula $-SiR^aR^bR^c$, in which R^a, R^b and R^c are alkyl or aryl, alkoxymethyl, (alkoxyalkoxy)methyl, haloalkoxymethyl, aralkyl, aryl or alkanoyloxymethoxycarbonyl; R^5 is carboxy or $-CONR^8R^9$, wherein R^8 and R^9 hydrogens or alkyl, or R^8 and R^9 together form alkylene; R^6 is hydrogen, alkyl, alkoxy or halogen; R^7 is carboxy or tetrazol-5-yl; $R_p^{\ 1}$ is hydrogen, alkyl, cycloalkyl or alkanoyl; $R_p^{\ 2}$ is a single bond, alkylene or alkylidene; $R_p^{\ 3}$ and $R_p^{\ 4}$ are each hydrogen or alkyl; $R_p^{\ 6}$ is carboxy or tetrazol-5-yl; and X_p is oxygen or sulfur; and pharmaceutically acceptable salts and esters thereof. The compounds are AII receptor antagonists and thus have hypotensive activity and can be used for the treatment and prophylaxis of hypertension. The compounds may be prepared by reacting a biphenylmethyl compound with an imidazole compound.

42 Claims, No Drawings

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ANGIOTENSIN II ANTAGOSIST 1-BIPHENYLMETHYLIMIDAZOLE COMPOUNDS AND THEIR THERAPEUTIC USE

CROSS REFERENCE TO RELATED APPLICATION

This is a continuation-in-part application of application Ser. No. 07/839,482, filed Feb. 20, 1992 and application Ser. No. 08/069,595, filed Jun. 1, 1993, both now abandoned.

BACKGROUND TO THE INVENTION

The present invention provides a series of novel 1-(biphenylmethyl)imidazole compounds which are antagonists to angiotension II (hereinafter referred to as "AII"). These compounds have valuable hypotensive activities, and which may, therefore, be used in the treatment and prophylaxis of hypertension, including diseases of the heart and circulatory system. The invention also provides methods and compositions using these compounds, as well as processes for their preparation.

It is known that the renin-angiotension system provides one of the important mechanisms for maintaining the homeostasis of blood pressure in living animals. When blood pressure is reduced or the sodium ion concentration of the body fluids falls, this system is activated. As a result, the enzyme renin and angiotensin converting enzyme (hereinafter abbreviated, as is conventional, as "ACE") are activated and act on angiotensinogen, which is first decomposed by the renin to produce angiotensin I (hereinafter abbreviated as "AI"). This AI is then converted by ACE to AII. Since AII induces strong contractions of blood vessels and accelerates the secretion of aldosterone (which is a hormone produced by the adrenal glands that controls the excretion of sodium by the kidneys and thereby maintains the balance of salt and water in the body fluids), the activation of the system results in an elevation of blood pressure. Inhibitors or suppressors of the renin-angiotension system, such as renin inhibitors, ACE inhibitors and AII antagonists, dilate blood vessels, cause lower blood pressure and improve the circulatory function, which is the basis for the use of these agents in the treatment of heart diseases.

At present only ACE inhibitors are used clinically, although renin inhibitors and AII antagonists are under investigation for such use. Of these, some peptide type AII antagonists, such as saralasin, have been known for many years, while certain non-peptide type antagonists have recently been discovered (for example, European Patent Publications No. 28 833, 28 834, 245 637, 253 310, 323 841, 324 377, 380 959, 399 732, 399 731, 400 835 and 492 105 and in Japanese Patent Application Kokai No. Sho 57-98270). Close prior art is considered to be European Patent Publications No. 253 310 and 324 377 and German Patent Publication 4 036 706.

European Patent Publication No. 253 310 discloses a series of 1-phenyl, 1-phenethyl or 1-benzyl imidazole derivatives which are said to have the ability to inhibit the activity of AII. Included in the scope of these prior art compounds are a number of 1-biphenylmethylimidazole derivatives, which, however, differ from the compounds of the present invention in the nature of the substituent at the imidazole 4- or 5- position.

European Patent Publication No. 324 377 discloses a series of 1-(substituted phenyl)-, 1-(substituted phenethyl)- or 1-(substituted benzyl)- imidazole derivatives which are

said to have the ability to inhibit the activity of AII. Included in the scope of these prior art compounds are a number of 1-biphenylmethylimidazole derivatives, which, however, differ from the compounds of the present invention in the nature of the substituent at the imidazole 4-position.

German Patent Publication No. 4 036 706 also discloses a series of such compounds, differing from the compounds of the present invention in a similar manner. The activities of all of these prior art compounds, however, including those of European Patent Publications No. 253310 and 324 377 and German Patent Publication No. 4 036 706, are not sufficient and more potent AII antagonists are sought for better clinical results.

We have now discovered a limited series of 1-(biphenylmethyl)imidazole-5-carboxylic acid derivatives, including compounds with specific substituents at the imidazole 4-position having an excellent AII receptor antagonist activity, and which are therefore useful as antihypertensive drugs and for the therapy and prophylaxis of heart diseases.

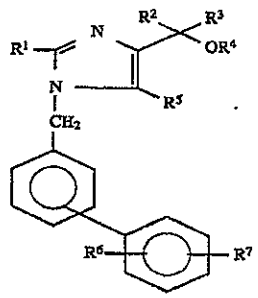
BRIEF SUMMARY OF INVENTION

It is, therefore, an object of the present invention provide a series of new 1-(biphenylmethyl)imidazole-5-carboxylic acid derivatives.

It is a further object of the invention to provide such compounds having AII inhibitory activity.

Other objects and advantages of the present invention will become apparent as the description proceeds.

Thus, the present invention provides compounds of formula (I):



(I)

wherein:

R^1 represents an alkyl group having from 1 to 6 carbon atoms or an alkenyl group having from 3 to 6 carbon atoms;

R^2 and R^3 are independently selected from the group consisting of:
- hydrogen atoms;
- alkyl groups having from 1 to 6 carbon atoms;
- alkenyl groups having from 3 to 6 carbon atoms;
- cycloalkyl groups having a total of from 3 to 10 carbon atoms in one or more saturated carbocyclic rings;
- aralkyl groups in which the alkyl part has from 1 to 6 carbon atoms and the aryl part is as defined below;
- aryl groups as defined below; and
- fused ring systems in which an aryl group, as defined below, is fused to a cycloalkyl group having from 3 to 10 carbon atoms;

R^4 represents:
- a hydrogen atom;
- an alkyl group having from 1 to 6 carbon atoms;
- an alkanoyl group having from 1 to 6 carbon atoms;

a substituted alkanoyl group having from 2 to 6 carbon atoms and substituted by at least one substituent selected from the group consisting of halogen atoms and alkoxy groups having from 1 to 6 carbon atoms;

an alkenoyl group having from 3 to 6 carbon atoms;

an arylcarbonyl group in which the aryl part is as defined below;

an alkoxycarbonyl group in which the alkyl part has from 1 to 6 carbon atoms;

a tetrahydropyranyl, tetrahydrothiopyranyl, tetrahydrothienyl or tetrahydrofuryl group;

a substituted tetrahydropyranyl, tetrahydrothiopyranyl, tetrahydrothienyl or tetrahydrofuryl group which is substituted by at least one substituent selected from the group consisting of halogen atoms and alkoxy groups having from 1 to 6 carbon atoms; a group of formula $-SiR^aR^bR^c$, in which 1, 2 or 3 of the groups represented by R^a, R^b and R^c are independently selected from the group consisting of alkyl groups having from 1 to 6 carbon atoms, and 2, 1 or 0 of the groups represented by R^a, R^b and R^c are independently selected from the group consisting of aryl groups, as defined below; alkoxymethyl groups in which the alkoxy part has from 1 to 6 carbon atoms;

(alkoxyalkoxy)methyl groups in which each alkoxy part has from 1 to 6 carbon atoms;

haloalkoxymethyl groups in which the alkoxy part has from 1 to 6 carbon atoms;

aralkyl groups, in which an alkyl group having from 1 to 6 carbon atoms is substituted by at least one aryl group, as defined below; or

alkanoyloxymethoxycarbonyl groups in which the alkanoyl part has from 1 to 6 carbon atoms;

R^5 represents a carboxy group or a group of formula $-CONR^8R^9$, wherein R^8 and R^9 are independently selected from the group consisting of

hydrogen atoms,

unsubstituted alkyl groups having from 1 to 6 carbon atoms, and

substituted alkyl groups which have from 1 to 6 carbon atoms and which are substituted by at least one substituent selected from the group consisting of substituents (a), defined below, or

R^8 and R^9 together represent an unsubstituted alkylene group having from 2 to 6 carbon atoms or a substituted alkylene group which has from 2 to 6 carbon atoms and which is substituted by at least one substituent selected from the group consisting of carboxy groups and alkoxycarbonyl groups in which the alkyl part has from 1 to 6 carbon atoms;

R^6 represents a hydrogen atom, an alkyl group having from 1 to 6 carbon atoms, an alkoxy group having from 1 to 6 carbon atoms or a halogen atom;

R^7 represents a carboxy group or a tetrazol-5-yl group;

said substituents (a) are selected from the group consisting of:

aryl groups as defined below;

heterocyclic groups having 5 or 6 ring atoms, of which from 1 to 4 are hetero-atoms selected from the group consisting of nitrogen, oxygen and sulfur atoms;

halogen atoms;

hydroxy groups;

alkoxy groups having from 1 to 6 carbon atoms;

carboxy groups

alkoxycarbonyl groups in which the alkyl part has from 1 to 6 carbon atoms;

amino groups; and

acylamino groups, in which the acyl part is an alkanoyl group having from 1 to 6 carbon atoms or an arylcarbonyl group, in which the aryl part is as defined below;

said aryl groups are aromatic carbocyclic groups which have from 6 to 14 ring atoms and which are unsubstituted or are substituted by at least one substituent selected from the group consisting of substituents (b), defined below; and

said substituents (b) are selected from the group consisting of nitro groups, cyano groups, halogen atoms, unsubstituted carbocyclic aryl groups having from 6 to 10 ring atoms, alkyl groups having from 1 to 6 carbon atoms, alkoxy groups having from 1 to 6 carbon atoms, carboxy groups, alkoxycarbonyl groups in which the alkoxy part has from 1 to 6 carbon atoms and alkylenedioxy and alkylidene- dioxy groups having from 1 to 3 carbon atoms;

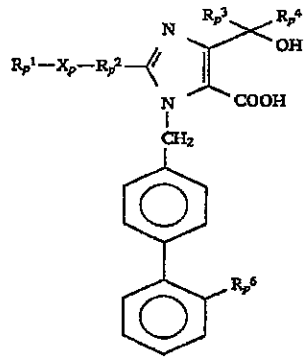
and pharmaceutically acceptable salts and esters thereof.

The invention also provides a pharmaceutical composition for the treatment or prophylaxis of hypertension, which comprises an effective amount of an anti-hypertensive agent in admixture with a pharmaceutically acceptable carrier or diluent, wherein the anti-hypertensive agent is selected from the group consisting of compounds of formula (I) and pharmaceutically acceptable salts and esters thereof.

The invention further provides a method for the treatment or prophylaxis of hypertension in a mammal, e.g. a human being, which comprises administering an effective amount of an anti-hypertensive agent to said mammal, wherein the anti-hypertensive agent is selected from the group consisting of compounds of formula (I) and pharmaceutically acceptable salts and esters thereof.

The invention still further provides processes for the preparation of compounds of formula (I) and pharmaceutically acceptable salts and esters thereof, which are described in more detail hereafter.

In accordance with the present invention, there are also provided compounds of formula $(I)_p$:



$(I)_p$

in which:

R_p^1 represents a hydrogen atom, an alkyl group having from 1 to 6 carbon atoms, a cycloalkyl group having from 3 to 6 ring carbon atoms or an alkanoyl group having from 1 to 6 carbon atoms;

R_p^2 represents a single bond or an alkylene or alkylidene group having from 1 to 4 carbon atoms;

R_p^3 R_p^4 are independently selected from the group consisting of hydrogen atoms and alkyl groups having from 1 to 6 carbon atoms;

R_p^6 represents a carboxy group or a tetrazol-5-yl group; and

X_p represents an oxygen or sulfur atom;

and pharmaceutically acceptable salts and esters thereof.

The invention also provides a pharmaceutical composition for the treatment or prophylaxis of hypertension or of a cardiovascular disease, which comprises an effective amount of an anti-hypertensive agent in admixture with a pharmaceutically acceptable carrier or diluent, wherein the anti-hypertensive agent is selected from the group consisting of compounds of formula $(I)_p$ and pharmaceutically acceptable salts and esters thereof.

The invention further provides a method for the treatment or prophylaxis of hypertension or of a cardiovascular disease in a mammal, e.g. a human being, which comprises administering an effective amount of an anti-hypertensive agent to said mammal, wherein the anti-hypertensive agent is selected from the group consisting of compounds of formula $(I)_p$ and pharmaceutically acceptable salts and esters thereof.

The invention still further provides processes for the preparation of compounds of formula $(I)_p$ and pharmaceutically acceptable salts and esters thereof, which are described in more detail hereafter.

DETAILED DESCRIPTION OF INVENTION

In the compounds of the present invention, where R^1, R^2, R^3, R^4, R^6, R^8, R^9 or substituent (b) is an alkyl group, this is an alkyl group having from 1 to 6 carbon atoms, and may be a straight or branched chain group having from 1 to 6 carbon atoms; examples include the methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, t-butyl, pentyl, t-pentyl, 2-methylbutyl, 3-methylbutyl, 1-ethylpropyl, 4-methylpentyl, 3-methylpentyl, 2-methylpentyl, 1-methylpentyl, 3,3-dimethylbutyl, 2,2-dimethylbutyl, 1,1-dimethylbutyl, 1,2-dimethylbutyl, 1,3-dimethylbutyl, 2,3-dimethylbutyl, 2-ethylbutyl, hexyl and isohexyl groups. R^1 preferably represents a straight or branched chain alkyl group containing from 2 to 5 carbon atoms, and more preferably a straight chain group, i.e. most preferably an ethyl, propyl or butyl group. Each of R^2 and R^3, which may be the same or different, preferably represents a straight or branched chain alkyl group containing from 1 to 4 carbon atoms, more preferably a methyl, ethyl, propyl, isopropyl or t-butyl group, and most preferably a methyl or ethyl group when R^5 represents a carboxy group, or an isopropyl or t-butyl group when R^5 represents a group of formula —$CONR^8R^9$. R^4 or R^6 preferably represents a straight or branched chain alkyl group containing from 1 to 4 carbon atoms, more preferably a methyl or ethyl group. Where R^8 and R^9 are alkyl groups, these may be the same or different, and each is preferably an alkyl group containing from 1 to 4 carbon atoms, more preferably a methyl, ethyl, propyl or butyl group, and most preferably a methyl or ethyl group. In the case of substituent (b), when this represents an alkyl group, it preferably has from 1 to 4 carbon atoms, and the methyl and ethyl groups are more preferred.

Where R^1, R^2 and R^3 represents an alkenyl group, this may be a straight or branched chain alkenyl group containing from 3 to 6 carbon atoms. Examples of such groups include: the 1-propenyl, 2-propenyl, 1-methyl-2-propenyl, 2-methyl-1-propenyl, 2-methyl-2-propenyl, 2-ethyl-2-propenyl, 1-butenyl, 2-butenyl, 1-methyl-2-butenyl, 2-methyl-2-butenyl, 3-methyl-2-butenyl, 1-ethyl-2-butenyl, 3-butenyl, 1-methyl-3-butenyl, 2-methyl-3-butenyl, 1-ethyl-3-butenyl, 1-pentenyl, 2-pentenyl, 1-methyl-2-pentenyl, 2-methyl-2-pentenyl, 3-pentenyl, 1-methyl-3-pentenyl, 2-methyl-3-pentenyl, 4-pentenyl, 1-methyl-4-pentenyl, 2-methyl-4-pentenyl, 1-hexenyl, 2-hexenyl, 3-hexenyl, 4-hexenyl and 5-hexenyl groups. R^1 preferably represents a straight or branched chain alkenyl group containing 3 or 4 carbon atoms, and more preferably a 1-propenyl or 1-butenyl group. Each of R^2 and R^3, which may be the same or different, preferably represents a straight or branched chain alkenyl group containing 3 or 4 carbon atoms, and more preferably a 2-propenyl or 2-butenyl group.

Where R^2 or R^3 represents a cycloalkyl group, this has a total of from 3 to 10 carbon atoms in one or more saturated carbocyclic rings, and the or each ring preferably has from 3 to 6 carbon atoms. Where the group is a multiple ring system, this may be a bridged or fused ring system. Examples of such groups include the cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, norbornyl and adamantyl groups. Of these, we prefer those groups having from 3 to 6 carbon atoms in a single ring, and most prefer the cyclopentyl and cyclohexyl groups.

Alternatively R^2, or R^3 may represent an aralkyl group, in which the alkyl part has from 1 to 6 (more preferably from 1 to 4, still more preferably 1 or 2, and most preferably 1) carbon atoms and the aryl part is an aromatic carbocyclic groups which has from 6 to 14 (preferably from 6 to 10, and more preferably 6 or 10) ring atoms and which is unsubstituted or is substituted by at least one substituent selected from the group consisting of substituents (b), defined above and exemplified below. Specific examples of alkyl groups which may form the alkyl part are as given above in relation to the alkyl groups which may be represented by R^2, and specific examples of the aryl groups which may form the aryl part are as given below in relation to the aryl groups which may be represented by R^2. Examples of such aralkyl groups include the benzyl, 1- and 2-naphthylmethyl, indenylmethyl, phenanthrenylmethyl, anthracenylmethyl, diphenylmethyl, triphenylmethyl, 1-phenylethyl, phenethyl, 1-naphthylethyl, 2-naphthylethyl, 1-phenylpropyl, 2-phenylpropyl, 3-phenylpropyl, 1-naphthylpropyl, 2-naphthylpropyl, 3-naphthylpropyl, 1-phenylbutyl, 2-phenylbutyl, 3-phenylbutyl, 4-phenylbutyl, 1-naphthylbutyl, 2-naphthylbutyl, 3-naphthylbutyl, 4-naphthylbutyl, 1-phenylpentyl, 2-phenylpentyl, 3-phenylpentyl, 4-phenylpentyl, 5-phenylpentyl, 1-naphthylpentyl, 2-naphthylpentyl, 3-naphthylpentyl, 4-naphthylpentyl, 5-naphthylpentyl, 1-phenylhexyl, 2-phenylhexyl, 3-phenylhexyl, 4-phenylhexyl, 5-phenylhexyl, 6-phenylhexyl, 1-naphthylhexyl, 2-naphthylhexyl, 3-naphthylhexyl, 4-naphthylhexyl, 5-naphthylhexyl and 6-naphthylhexyl groups. In those cases where the aralkyl group contains a naphthyl group, this may be a 1- or 2-naphthyl group. Of these aralkyl groups, we prefer those groups in which the alkyl part has from 1 to 4 carbon atoms, the benzyl group being most preferred. These groups may be unsubstituted or they may be substituted by one or more of substituents (b), defined above and exemplified below. Examples of the substituted groups include those unsubtituted groups exemplified above but in which the aryl part is replaced by one of the substituted aryl groups given below. However, the unsubtituted groups are preferred.

Where R^2 or R^3 represents an aryl group, this is an aromatic carbocyclic group which has from 6 to 14 (preferably from 6 to 10, and more preferably 6 or 10) ring atoms and which is unsubstituted or is substituted by at least one substituent selected from the group consisting of substituents (b), defined above and exemplified below. Such groups may be unsubtituted or they may be substituted by at least one, and preferably from 1 to 3, of substituents (b), for example:

nitro groups;

cyano groups;

halogen atoms, such as the fluorine, chlorine, bromine or iodine atoms, of which the fluorine, chlorine and bromine atoms are preferred;

unsubstituted carbocyclic aryl groups, e.g. as exemplified below in relation to R^2 and R^3;

alkyl groups, as exemplified above, most preferably the methyl group;

alkoxy groups having from 1 to 6, preferably from 1 to 4, carbon atoms, such as the methoxy, ethoxy, propoxy, isopropoxy, butoxy, isobutoxy, sec-butoxy, t-butoxy, pentyloxy, neopentyloxy, 2-methylbutoxy-, 3-methylbutoxy, 1-ethylpropoxy, 4-methylpentyloxy, 3-methylpentyloxy, 2-methylpentyloxy, 1-methylpentyloxy, 3,3-dimethylbutoxy, 2,2-dimethylbutoxy, 1,1-dimethylbutoxy, 1,2-dimethylbutoxy, 1,3-dimethylbutoxy, 2,3-dimethylbutoxy, 2-ethylbutoxy, hexyloxy and isohexyloxy groups, most preferably a methoxy or ethoxy group;

alkoxycarbonyl groups in which the alkoxy part has from 1 to 6, preferably from 1 to 4, carbon atoms, such as the methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, isopropoxycarbonyl, butoxycarbonyl, isobutoxycarbonyl, t-butoxycarbonyl, pentyloxycarbonyl and hexyloxycarbonyl groups, of which the methoxycarbonyl and ethoxycarbonyl groups are most preferred;

carboxy groups;

alkylenedioxy and alkylidenedioxy groups having from 1 to 3 carbon atoms, for example the methylenedioxy, ethylenedioxy, propylenedioxy, trimethylenedioxy, ethylidenedioxy and isopropylidenedioxy groups, of which the methylenedioxy group is most preferred.

Of these, the alkyl and alkoxy substituents are preferred where R^2 or R^3 represents a substituted aryl group.

Where the group is substituted, the number of substituents is not critical, and is only limited by the number of substitutable positions, and possibly by steric constraints. However, in practice, we normally prefer 1, 2 or 3 substituents.

Examples of substituted and unsubstituted aryl groups include the phenyl, naphthyl, phenanthrenyl, anthracenyl, 2-methylphenyl, 3-methylphenyl, 4-methylphenyl, 2-ethylphenyl, 3-propylphenyl, 4-ethylphenyl, 2-butylphenyl, 3-pentylphenyl, 4-pentylphenyl, 3,5-dimethylphenyl, 2,5-dimethylphenyl, 2,6-dimethylphenyl, 2,4-dimethylphenyl, 3,5-dibutylphenyl, 2,5-dipentylphenyl, 2,6-dipropyl-4-methylphenyl, 2-methoxyphenyl, 3-methoxyphenyl, 4-methoxyphenyl, 2-ethoxyphenyl, 3-propoxyphenyl, 4-ethoxyphenyl, 2-butoxyphenyl, 3-pentyloxyphenyl and 4-pentyloxyphenyl groups, of which the phenyl, 2-methylphenyl, 3-methylphenyl, 4-methylphenyl, 2-methoxyphenyl, 3-methoxyphenyl and 4-methoxyphenyl groups are the most preferred.

Where R^2 or R^3 represents a fused ring system in which an aryl group is fused to a cycloalkyl group having from 3 to 10 carbon atoms, the aryl and cycloalkyl parts may be as exemplified above, and preferably the aryl part is a phenyl or naphthyl group, and the cycloalkyl part has 5 or 6 carbon atoms. Examples of such fused ring systems include the indanyl, tetrahydronaphthyl and tetrahydroanthryl groups, of which the indanyl and tetrahydronaphthyl groups are preferred.

R^4 can represent an alkanoyl group; such a group may be a straight or branched chain group and has from 1 to 6 carbon atoms. Examples of such groups include the formyl, acetyl, propionyl, butyryl, isobutyryl, pivaloyl, valeryl and isovaleryl groups, of which the formyl and acetyl groups are preferred.

Alternatively, R^4 may be a substituted alkanoyl group in which the substituent or substituents is or are selected from the group consisting of the halogen atoms and the alkoxy groups. Examples of such substituted alkanoyl groups include the chloroacetyl, dichloroacetyl, trichloroacetyl, trifluoroacetyl and methoxyacetyl groups, of which the chloroacetyl and trifluoroacetyl groups are preferred.

Where R^4 represents an alkenoyl group, this may have from 3 to 6, preferably from 3 to 5, carbon atoms, and examples include the acryloyl, methacryloyl, crotonoyl, 3-methyl-2-butenoyl and 2-methyl-2-butenoyl, especially (E)-2-methyl-2-butenoyl, groups.

Where R^4 represents an arylcarbonyl group, the aryl part may be any of those aryl groups exemplified above in relation to R^2. However, in this case, if the group is substituted, the substituents are preferably selected from the group consisting of halogen atoms, alkyl groups, alkoxy groups, nitro groups, alkoxycarbonyl groups and unsubstituted aryl groups, more preferably the methyl, methoxy, fluoro and chloro substituents. Examples of the arylcarbonyl groups include the benzoyl, α-naphthoyl, β-naphthoyl, 3-fluorobenzoyl, 2-bromobenzoyl, 4-chlorobenzoyl, 2,4,6-trimethylbenzoyl, 4-toluoyl, 4-anisoyl, 4-nitrobenzoyl, 2-nitrobenzoyl, 2-(methoxycarbonyl)benzoyl and 4-phenylbenzoyl groups, of which the benzoyl, 4-toluoyl, and 4-anisoyl groups are preferred.

Where R^4 represents an alkoxycarbonyl group, the alkoxy part has from 1 to 6 carbon atoms, i.e. the group as a whole has from 2 to 7 carbon atoms, and examples of such groups include the methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, isopropoxycarbonyl, butoxycarbonyl, isobutoxycarbonyl, t-butoxycarbonyl, pentyloxycarbonyl and hexyloxycarbonyl groups, of which the methoxycarbonyl and ethoxycarbonyl groups are preferred.

Where R^4 represents a tetrahydropyranyl, tetrahydrothiopyranyl, tetrahydrothienyl or tetrahydrofuryl group, this may be substituted or unsubstituted. If substituted, the substituents are selected from the group consisting of halogen atoms and alkoxy groups having from 1 to 6 carbon atoms, which may be any of those groups and atoms exemplified above in relation to R^4, preferably the chloro, bromo and methoxy substituents. Examples of these substituted and unsubstituted groups include the tetrahydropyran-2-yl, 3-chlorotetrahydropyran-2-yl, 3-bromotetrahydropyran-2-yl, 4-methoxytetrahydropyran-2-yl, tetrahydrothiopyran-2-yl, 4-methoxytetrahydrothiopyran-2-yl, tetrahydrofuran-2-yl and tetrahydrothien-2-yl groups, of which the tetrahydropyran-2-yl, 4-methoxytetrahydropyran-2-yl, tetrahydrothiopyran-2-yl and 4-methoxytetrahydrothiopyran-2yl groups are preferred.

Where R^4 represents a silyl group of formula —$SiR^aR^bR^c$ in which 1, 2 or 3 of the groups represented by R^a, R^b and R^c are independently selected from the group consisting of alkyl groups having from 1 to 6 carbon atoms, and 2, 1 or 0 of the groups represented by R^a, R^b and R^c are independently selected from the group consisting of aryl groups, as defined above, the alkyl and aryl parts may be any of those groups exemplified above in relation to R^1 and R^2, preferably the methyl, ethyl, t-butyl and phenyl groups. Examples of such silyl groups include the trimethylsilyl, triethylsilyl, isopropyldimethylsilyl, t-butyldimethylsilyl, methyldiisopropylsilyl, methyl-di-t-butylsilyl, triisopropylsilyl, diphenylmethylsily, diphenylbutylsilyl, diphenylisopropylsilyl and phenyldiisopropylsilyl groups, of which the trimethylsilyl, t-butyldimethylsilyl and diphenylmethylsilyl groups are preferred.

Where R^4 represents an alkoxymethyl group in which the alkoxy part has from 1 to 6 carbon atoms, the alkoxy part may be any of the alkoxy groups exemplified above in relation to substituents (b). Examples of such alkoxymethyl groups include the methoxymethyl, 1,1-dimethyl-1-methoxymethyl, ethoxymethyl, propoxymethyl, isopropoxymethyl, butoxymethyl and t-butoxymethyl groups, of which the methoxymethyl and ethoxymethyl groups are preferred.

Where R^4 represents an (alkoxyalkoxy)methyl group, each alkoxy part has from 1 to 6 carbon atoms and may be any of the alkoxy groups exemplified above in relation to substituents (b). Examples of such (alkoxyalkoxy)methyl groups include the methoxymethoxymethyl, 2-methoxyethoxymethyl, 2-methoxypropoxymethyl and 2-methoxybutoxymethyl groups, of which the 2-methoxyethoxymethyl group is preferred.

Where R^4 represents a haloalkoxymethyl group, the alkoxy part has from 1 to 6 carbon atoms and the halogen atoms and alkoxy groups may be any of the atoms and groups exemplified above in relation to substituents (b). Examples of such haloalkoxymethyl groups include the 2,2,2-trichloroethoxymethyl, 2,2,2-tribromoethoxymethyl, bis(2-chloroethoxy)methyl and bis(2-bromoethoxy)methyl groups, of which the 2,2,2-trichloroethoxymethyl and bis(2-chloroethoxy)methyl groups are preferred.

Where R^4 represents an aralkyl group, in which an alkyl group having from 1 to 6, preferably from 1 to 4, carbon atoms is substituted by at least one aryl group, the alkyl and aryl parts may be any of the alkyl and aryl groups exemplified above in relation to R^1 and R^2. Examples of such aralkyl groups include the benzyl, α-naphthylmethyl, β-naphthylmethyl, diphenylmethyl(benzhydryl), trityl, α-naphthyldiphenylmethyl, 9-anthrylmethyl, 4-methylbenzyl, 6-phenylhexyl, 2,4,6-trimethylbenzyl, 3,4,5-trimethylbenzyl, 4-methoxybenzyl, 4-methoxyphenyldiphenylmethyl, 2-nitrobenzyl, 4-nitrobenzyl, 4-chlorobenzyl, 4-bromobenzyl and 4-cyanobenzyl groups, of which the benzyl, 4-methylbenzyl, 4-methoxybenzyl, 4-chlorobenzyl and 4-bromobenzyl groups are preferred.

Where R^4 represents an alkanoyloxymethoxycarbonyl group, the alkanoyl part has from 1 to 6 carbon atoms and may be any of the alkanoyl groups exemplified above in relation to R^4. Examples of such alkanoyloxymethoxycarbonyl groups include the formyloxymethoxycarbonyl, acetoxymethoxycarbonyl, propionyloxymethoxycarbonyl, butyryloxymethoxycarbonyl and pivaloyloxymethoxycarbonyl groups, of which the pivaloyloxymethoxycarbonyl group is preferred.

R^5 represents a carboxy group or a group of formula $—CONR^8R^9$. Where it represents a group of formula $—CONR^8R^9$, and R^8 or R^9 represents an alkyl group, this may be an unsubstituted alkyl group having from 1 to 6 carbon atoms, such as those groups exemplified above, or a substituted alkyl group, which has from 1 to 6 carbon atoms and which is substituted by at least one substituent selected from the group consisting of substituents (a), defined above and exemplified below.

Where R^8 and R^9 together represent an alkylene group, this has from 2 to 6 carbon atoms and may be substituted or unsubstituted; it may also be a straight or branched chain group. Examples of the unsubstituted groups include the ethylene, trimethylene, propylene, ethylethylene, tetramethylene, pentamethylene and hexamethylene groups, of which those groups containing 4 or 5 carbon atoms are preferred. In such cases, the group of formula $—NR^8R^9$ is a nitrogen-containing heterocyclic group having from 3 to 7 ring atoms (one being the nitrogen atom), for example, when the alkylene group contains 4 or 5 carbon atoms, it is a 1-pyrrolidinyl or piperidino group, respectively. Where the group is substituted, there may be one or more substituents selected from the group consisting of carboxy groups and alkoxycarbonyl groups in which the alkoxy part has from 1 to 6 carbon atoms. Examples of such substituents include the carboxy, methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, butoxycarbonyl, isobutoxycarbonyl, t-butoxycarbonyl, pentyloxycarbonyl and hexyloxycarbonyl groups, of which the carboxy, methoxyarbonyl and ethoxycarbonyl groups are preferred.

Where R^5 represents a carboxy group, the compound is a carboxylic acid and can, therefore, form esters, in which the carboxy group represented by R^5 is replaced by a group of formula $—COOR^{5a}$, in which R^{5a} represents an ester residue (in the case of the carboxylic acid, R^{5a} represents a hydrogen atom). It can also form salts, examples of which are as exemplified below in relation to R^7. The nature of the ester so formed is not critical to the invention, except where the ester is to be used for pharmaceutical purposes, in which case it should be pharmaceutically acceptable, i.e. it should not have increased, or unacceptably increased, toxicity or reduced, or unacceptably reduced, activity, as compared with the parent acid. However, where the ester is to be used for other purposes, e.g. as intermediates for the preparation of other, and perhaps more active, compounds, even this restriction does not apply, and any ester residue common in the art may be used and may be selected on the basis of its functionality and commercial advantages. However, it is well known in the art that certain ester residues confer advantages on compounds incorporating them, for example easier or better absorption in vivo, and, if desired, such ester residues may be used in the present invention.

Examples of such ester residues include:

alkyl groups having from 1 to 6 carbon atoms, such as those exemplified above in relation to R^1;

haloalkyl groups having from 1 to 6, preferably from 1 to 4, carbon atoms, in which the alkyl part may be as exemplified above in relation to R^1, for example the trifluoromethyl, 2,2,2-trichloroethyl, 2,2,2-trifluoroethyl, 2-chloroethyl, 2-fluoroethyl, 2-iodoethyl, 4-fluorobutyl, 3-chloropropyl and 6-iodohexyl groups, of which the 2,2,2-trichloroethyl and 2-chloroethyl groups are preferred;

hydroxyalkyl groups having from 1 to 6, preferably from 1 to 4, carbon atoms, in which the alkyl part may be as exemplified above in relation to R^1, for example the 2-hydroxyethyl, 2,3-dihydroxypropyl, 3-hydroxypropyl, 3,4-dihydroxybutyl and 4-hydroxybutyl groups, of which the 2-hydroxyethyl group is preferred;

alkoxyalkyl and alkoxyalkoxyalkyl groups in which the alkoxy and the alkyl parts each have from 1 to 6, preferably from 1 to 4, carbon atoms, and may be as exemplified above in relation to substituents (b) and R^1, respectively, for example the methoxymethyl, 2-methoxyethyl, 2-ethoxyethyl and 2-methoxyethoxymethyl groups, of which the methoxymethyl group is preferred;

phenacyl groups and phenacyl groups which are substituted by one or more of substituents (b), of which the unsubstituted phenacyl group is preferred;

alkoxycarbonylalkyl groups, such as the methoxycarbonylmethyl group;

cyanoalkyl groups having from 1 to 6, preferably from 1 to 4, carbon atoms, in which the alkyl part may be as exemplified above in relation to R^1, for example the 2-cyanoethyl and cyanomethyl groups;

alkylthioalkyl groups in which each alkyl part has from 1 to 6, preferably from 1 to 4, carbon atoms, and may be as exemplified above in relation to R^1, for example the methylthiomethyl and ethylthiomethyl;

arylthioalkyl groups in which the alkyl part has from 1 to 6, preferably from 1 to 4, carbon atoms, and may be as exemplified above in relation to R^1, and the aryl part may be as defined and exemplified above in relation to R^2, for example the phenylthiomethyl group;

alkylsulfonylalkyl groups in which each alkyl part has from 1 to 6, preferably from 1 to 4, carbon atoms, and may be as exemplified above in relation to R^1 and may be unsubstituted or substituted by one or more halogen atoms, for example the 2-(methanesulfonyl)ethyl or 2-(trifluoromethanesulfonyl)ethyl groups;

arylsulfonylalkyl groups in which the alkyl part has from 1 to 6, preferably from 1 to 4, carbon atoms, and may be as exemplified above in relation to R^1, and the aryl part may be as defined and exemplified above in relation to R^2, for example the 2-(benzenesulfonyl) ethyl and 2-(p-toluenesulfonyl)ethyl groups;

aryl groups such as those exemplified above in relation to R^2;

aralkyl groups such as those exemplified above in relation to R^2, especially the benzyl, p-methoxybenzyl, p-nitrobenzyl and 4-acetoxy-3-methoxybenzyl groups, of which the benzyl group is preferred;

groups of formula —$SiR^dR^eR^f$ (in which R^d, R^e and R^f are as defined above in relation to R^a, R^b and R^c), such as those exemplified above in relation to R^4;

alkanoyloxyalkyl groups in which each of the alkanoyl and the alkyl parts has from 1 to 6 carbon atoms and may be as exemplified above in relation to R^1 and R^4, respectively, and preferably the alkanoyl part has from 1 to 5 carbon atoms and the alkyl part has from 1 to 4 carbon atoms and more preferably the alkanoyl part has from 2 to 5 carbon atoms and alkyl part has from 1 to 2 carbon atoms; examples of such alkanoyloxyalkyl groups include the formyloxymetnyl, acetoxymethyl, propionyloxymethyl, butyryloxymethyl, pivaloyloxymethyl, valeryloxymethyl, isovaleryloxymenty1, hexanoyloxymethyl, 1-(formyloxy)ethyl, 1-(acetoxy) ethyl, 1-(propionyloxy)ethyl, 1-(butyryloxy)ethyl, 1-(pivaloyloxy)ethyl, 1-(valeryloxy)ethyl, 1-(isovaleryloxy)ethyl, 1-(hexanoyloxy)ethyl, 2-(formyloxy) ethyl, 2-(acetoxy)ethyl, 2-(propionyloxy)ethyl, 2-(butyryloxy)ethyl, 2-(pivaloyloxy)ethyl, 2-(valeryloxy) ethyl, 2-(isovaleryloxy)ethyl, 2-(hexanoyloxy)ethyl, 1-(formyloxy)propyl, 1-(acetoxy)propyl, 1-(propionyloxy)propyl, 1-(butyryloxy)propyl, 1-(pivaloyloxy) propyl, 1-(valeryloxy)propyl, 1-(isovaleryloxy)propyl, 1-(hexanoyloxy)propyl, 1-(acetoxy) butyl, 1-(propionyloxy)butyl, 1-(butyryloxy)butyl, 1-(pivaloyloxy)butyl, 1-(acetoxy)pentyl, 1-(propionyloxy) pentyl, 1-(butyryloxy)pentyl, 1-(pivaloyloxy)pentyl and 1-(pivaloyloxy)hexyl groups, preferably the formyloxymethyl, acetoxymethyl, propionyloxymethyl, butyryloxymethyl, pivaloyloxymethyl, 1-(formyloxy) ethyl, 1-(acetoxy)ethyl, 1-(propionyloxy)ethyl, 1-(butyryloxy)ethyl and 1-(pivaloyloxy) ethyl groups, and more preferably the acetoxymethyl, propionyloxymethyl, butyryloxymethyl, pivaloyloxymethyl, 1-(acetoxy)ethyl, 1-(propionyloxy)ethyl, 1-(butyryloxy) ethyl and 1-(pivaloyloxy)ethyl groups and most preferably the pivaloyloxymethyl and 1-(pivaloyloxy) ethyl groups;

cycloalkanoyloxyalkyl groups in which the cycloalkyl part has 5 or 6 carbon atoms and the alkyl parts has from 1 to 6 carbon atoms, each as exemplified above in relation to R^2; preferably the alkyl part has from 1 to 4 carbon atoms and more preferably 1 or 2 carbon atoms; examples of such cycloalkanoyloxyalkyl groups include the cyclopentanoyloxymethyl, cyclohexanoyloxymethyl, 1-(cyclopentanoyloxy)ethyl, 1-(cyclohexanoyloxy)ethyl, 1-(cyclopentanoyloxy)propyl, 1-(cyclohexanoyloxy)propyl, 1-(cyclopentanoyloxy)butyl and 1-(cyclohexanoyloxy)butyl, groups, preferably the cyclopentanoyloxymethyl, cyclohexanoyloxymethyl, 1-(cyclopentanoyloxy)ethyl, and 1-(cyclohexanoyloxy)ethyl groups;

alkoxycarbonyloxyalkyl groups in which each of the alkoxy and the alkyl parts has from 1 to 6 carbon atoms as exemplified above in relation to substituents (b) and R^1, respectively, and preferably each of the alkoxy and the alkyl parts has from 1 to 4 carbon atoms and more preferably the alkoxy part has from 1 to 4 carbon atoms and alkyl part has from 1 to 2 carbon atoms; examples of such alkoxycarbonyloxyalkyl groups include the methoxycarbonyloxymethyl, ethoxycarbonyloxymethyl, propoxycarbonyloxymethyl, isopropoxycarbonyloxymethyl, butoxycarbonyloxymethyl, isobutoxycarbonyloxymethyl, pentyloxycarbonyloxymethyl, hexyloxycarbonyloxymethyl, 1-(methoxycarbonyloxy) ethyl, 1-(ethoxycarbonyloxy)ethyl, 1-(propoxycarbonyloxy)ethyl, 1-(isopropoxycarbonyloxy)ethyl, 1-(butoxycarbonyloxy)ethyl, 1-(isobutoxycarbonyloxy) ethyl, 1-(pentyloxycarbonyloxy)ethyl, 1-(hexyloxycarbonyloxy)ethyl, 2-(methoxycarbonyloxy)ethyl, 2-(ethoxycarbonyloxy)ethyl, 2-(propoxycarbonyloxy) ethyl, 2-(isopropoxycarbonyloxy)ethyl, 2- (butoxycarbonyloxy)ethyl, 2-(isobutoxycarbonyloxy) ethyl, 2-(pentyloxycarbonyloxy)ethyl, 2-(hexyloxycarbonyloxy)ethyl, 1-(methoxycarbonyloxy)propyl, 1-(ethoxycarbonyloxy)propyl, 1-(propoxycarbonyloxy) propyl, 1-(isopropoxycarbonyloxy)propyi, 1-(butoxycarbonyloxy)propyl, 1-(isobutoxy-carbonyloxy) propyl, 1-(pentyloxycarbonyloxy)propyl, 1-(hexyloxy carbonyloxy)propyl, 1-(methoxycarbonyloxy)butyl, 1-(ethoxycarbonyloxy)butyl, 1-(propoxycarbonyloxy) butyl, 1-(isopropoxycarbonyloxy)butyl, 1-(butoxycarbonyloxy)butyl, 1-(isobutoxycarbonyloxy)butyl, 1-(methoxycarbonyloxy)pentyl, 1-(ethoxycarbonyloxy)pentyl, 1-(methoxycarbonyloxy)hexyl and 1-(ethoxycarbonyloxy)hexyl groups, preferably the methoxycarbonyloxymethyl, ethoxycarbonyloxymethyl, propoxycarbonyloxymethyl, isopropoxycarbonyloxymethyl, butoxycarbonyloxymethyl, isobutoxycarbonyloxymethyl, 1-(methoxycarbonyloxy)ethyl, 1-(ethoxycarbonyloxy)ethyl, 1-(propoxycarbonyloxy) ethyl, 1-(isopropoxycarbonyloxy)ethyl, 1-(butoxycarbonyloxy)ethyl, 1-(isobutoxycarbonyloxy)ethyl, 1-(methoxycarbonyloxy)propyl, 1-(ethoxycarbonyloxy) propyl, 1-(propoxycarbonyloxy)propyl, 1-(isopropoxycarbonyloxy)propyl, 1-(butoxycarbonyloxy) propyl, 1-(isobutoxycarbonyloxy)propyl, 1-(methoxycarbonyloxy)butyl, 1-(ethoxycarbonyloxy) butyl, 1-(propoxycarbonyloxy)butyl, 1-(isopropoxycarbonyloxy)butyl, 1-(butoxycarbonyloxy)butyl, 1-(isobutoxycarbonyloxy)butyl, more preferably methoxycarbonyloxymethyl, ethoxycarbonyloxymethyl, propoxycarbonyloxymethyl, isopropoxycarbonyloxymethyl, butoxycarbonyloxymethyl, isobutoxycarbonyloxymethyl, 1-(methoxycarbonyloxy)ethyl,

1-(ethoxycarbonyloxy)ethyl, 1-(propoxycarbonyloxy) ethyl, 1-(isopropoxycarbonyloxy)ethyl, 1-(butoxycarbonyloxy)ethyl and 1-(isobutoxycarbonyloxy)ethyl groups and most preferably the methoxycarbonyloxymethyl, ethoxycarbonyloxymethyl, isopropoxycarbonyloxymethyl, 1-(methoxycarbonyloxy)ethyl, 1-(ethoxycarbonyloxy)ethyl and 1-(isopropoxycarbonyloxy)ethyl groups;

cycloalkoxycarbonyloxyalkyl groups in which the cycloalkyl part has 5 or 6 carbon atoms and the alkyl parts has from 1 to 6 carbon atoms, each as exemplified above in relation to R^2; preferably the alkyl part has from 1 to 4 carbon atoms and more preferably 1 or 2 carbon atoms; examples of such cycloalkoxycarbonyloxyalkyl groups include the cyclopentoxycarbonyloxymethyl, cyclohexyloxycarbonyloxymethyl, 1-(cyclopentyloxycarbonyloxy)ethyl, 1-(cyclohexyloxycarbonyloxy)ethyl, 1-(cyclopentyloxycarbonyloxy)propyl, 1-(cyclohexyloxycarbonyloxy)propyl, 1-(cyclopentyloxycarbonyloxy)butyl and 1-(cyclohexyloxycarbonyloxy)butyl groups, preferably the cyclopentyloxycarbonyloxymethyl, cyclohexyloxycarbonyloxymethyl, 1-(cyclopentoxycarbonyloxy) ethyl and 1-(cyclohexyloxycarbonyloxy)ethyl groups;

[5-(aryl- or alkyl-)-2-oxo-1,3-dioxolen-4-yl]methyl groups in which the alkyl part has from 1 to 6 carbon atoms and may be as exemplified above in relation to R^1 and R^2, and the aryl part is as defined and exemplified above in relation to R^2 (and is preferably a substituted or unsubstituted phenyl group); preferably the alkyl part has from 1 to 4 carbon atoms and more preferably 1 or 2 carbon atoms; examples of such [5-(aryl- or alkyl-)-2-oxo-1,3-dioxolen-4-yl]methyl groups include the (5-phenyl-2-oxo-1,3-dioxolen-4-yl) methyl, [5-(4-methylphenyl)-2-oxo-1,3-dioxolen-4-yl] methyl, [5-(4-methoxyphenyl)-2-oxo-1,3-dioxolen-4-yl]methyl, [5-(4-chlorophenyl)-2-oxo-1,3-dioxolen-4-yl]methyl, [5-(4-fluorophenyl)-2-oxo-1,3-dioxolen-4-yl]methyl, (5-methyl-2-oxo-1,3-dioxolen-4-yl)methyl, (5-ethyl-2-oxo-1,3-dioxolen-4-yl)methyl, (5-propyl-2-oxo-1,3-dioxolen-4-yl)methyl, (5-isopropyl-2-oxo-1,3-dioxolen-4-yl)methyl and (5-butyl-2-oxo-1,3-dioxolen-4-yl)methyl groups, preferably the (5-phenyl-2-oxo-1,3-dioxolen-4-yl)methyl, (5-methyl-2-oxo-1,3-dioxolen-4-yl)methyl and (5-ethyl -2-oxo-1,3-dioxolen-4-yl)methyl groups and more preferably the (5-methyl-2-oxo-1,3-dioxolen-4-yl)methyl group; and

phthalidyl groups.

Preferred ester residues are, for example:

C_1–C_4alkyl groups

phenyl, naphthyl and substituted phenyl groups having one or more, preferably from 1 to 3, methyl, ethyl, methoxy, ethoxy, fluoro and chloro substituents, which, in the case of 2 or 3 substituents, may be the same or different;

benzyl, diphenylmethyl and α- and β-naphthylmethyl groups, and substituted benzyl groups having one or more, preferably from 1 to 3, methyl, ethyl, methoxy, ethoxy, fluoro and chloro substituents, which, in the case of 2 or 3 substituents, may be the same or different;

groups of formula $SiR^dR^eR^f$ in which 1, 2 or 3 of the groups represented by R^d, R^e and R^f are independently selected from the group consisting of alkyl groups having from 1 to 4 carbon atoms, and 2, 1 or 0 are phenyl groups;

alkanoyloxyalkyl groups in which the alkanoyl group has from 1 to 5 carbon atoms and the alkyl group has from 1 to 4 carbon atoms;

cycloalkanoyloxyalkyl groups in which the cycloalkyl part has 5 or 6 carbon atoms and the alkyl part has from 1 to 4 carbon atoms;

alkoxycarbonyloxyalkyl groups in which each of the alkoxy part and the alkyl part has from 1 to 4 carbon atoms;

cycloalkoxycarbonyloxyalkyl groups in which the cycloalkyl part has 5 or 6 carbon atoms and the alkyl part has from 1 to 4 carbon atoms;

[5-(phenyl or alkyl-)-2-oxo-1,3-dioxolen-4-yl]methyl groups in which the alkyl part has from 1 to 4 carbon atoms; and

phthalidyl groups.

More preferred ester residues are, for example,

C_1–C_4 alkyl groups;

the benzyl group;

alkanoyloxyalkyl groups in which the alkanoyl part has from 1 to 5 carbon atoms and the alkyl part has 1 or 2 carbon atoms;

cycloalkanoyloxyalkyl groups in which the cycloalkyl part has from 5 to 6 carbon atoms and the alkyl part has 1 or 2 carbon atoms;

alkoxycarbonyloxyalkyl groups in which the alkoxy part has from 1 to 4 carbon atoms and alkyl part has 1 or 2 carbon atoms;

cycloalkoxycarboonyloxyalkyl groups in which the cycloalkyl part has 5 or 6 carbon atoms and the alkyl part has 1 or 2 carbon atoms;

[5-(phenyl or alkyl-)-2-oxo-1,3-dioxolen-4-yl]methyl groups in which the alkyl part has 1 or 2 carbon atoms; and

phthalidyl groups.

The most preferred ester residues are, for example, pivaloyloxymethyl, ethoxycarbonyloxymethyl, 1-(ethoxycarbonyloxy)ethyl, isopropoxycarbonyloxymethyl, (1-isopropoxycarbonyloxy)ethyl, (5-methyl-2-oxo-1,3-dioxolen-4-yl)methyl and phthalidyl groups.

Examples of the groups and atoms which may form substituents (a) include:

aryl groups, such as those exemplified above in relation to R^2;

heterocyclic groups having 5 or 6 ring atoms, of which from 1 to 4 are hereto-atoms selected from the group consisting of nitrogen, oxygen and sulfur atoms, and as exemplified below;

halogen atoms, alkoxy groups and alkoxycarbonyl groups, such as those exemplified in relation to substituents (b);

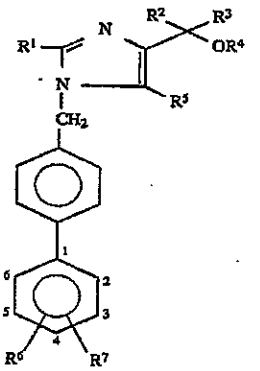
hydroxy groups, carboxy groups and amino groups; and

acylamino groups, in which the acyl part is an alkanoyl group having from 1 to 6 carbon atoms or an arylcarbonyl group, in which the aryl part is as defined above, of which the acyl part is as exemplified above in relation to R^4, e.g. a benzamido group, and preferably an alkanoylamino group having from 1 to 4 carbon atoms, and more preferably an acetamido or formamido group.

Where substituent (a) is a heterocyclic group, this has 5 or 6 ring atoms, of which from 1 to 4 are hereto-atoms selected from nitrogen, oxygen and sulfur hereto-atoms. Where there are 4 hereto-atoms, we prefer that all 4 should be nitrogen atoms. Where there are 3 hereto-atoms, we prefer that at least one (more preferably 2) should be a nitrogen atom and one or two should be nitrogen, oxygen or sulfur atoms (and,

where there are two, they may be the same or different). Where there are two hereto-atoms, these may be the same or different and they are selected from nitrogen, oxygen and sulfur atoms; however, more preferably one is a nitrogen atom or an oxygen atom and the other is a nitrogen, oxygen or sulfur atom. Examples of such heterocyclic groups include the pyrrolyl, furyl, thienyl, imidazolyl, oxazolyl, thiazolyl, oxadiazoiyl, thiadiazolyl, triazolyl, tetrazolyl and pyridyl groups (preferably a furyl, thienyl, imidazolyl, oxazolyl or thiazolyl group), preferably a furyl or thienyl group.

Preferably the benzene ring for formula (I) which bears the substituents represented by R^6 and R^7 is at the 3- or 4-position of the benzyl group to which it attaches, more preferably at the 4-position, i.e. the preferred compounds have the formula (Ia):



(Ia)

R^6 may represent a hydrogen atom, an alkyl group having from 1 to 6 carbon atoms (such as those exemplified above) or an alkoxy group having from 1 to 6 carbon atoms or a halogen atom, both of which are as exemplified above in relation to the same groups or atoms which may be represented by substituents (b). R^6 is preferably at the 6-position of the benzene ring.

R^7 may represent a carboxy group or a tetrazol-5-yl group. When it represents a carboxy group, or when substituent (a) is a carboxy group, the resulting compounds may form salts or esters. There is no particular restriction on the nature of these salts or esters, provided that, where they are intended for therapeutic use, they are pharmaceutically acceptable. Where they are intended for non-therapeutic uses, e.g. as intermediates in the preparation of other, and possibly more active, compounds, even this restriction does not apply. Examples of such salts include: salts with an alkali metal, such as sodium, potassium or lithium; salts with an alkaline earth metal, such as barium or calcium; salts with another metal, such as magnesium and aluminum; organic base salts, such as a salt with guanidine, triethylamine, dicyclohexylamine; and salts with a basic amino acid, such as lysine or arginine. Examples of ester groups may be as exemplified above in relation to R^{5a}.

Preferably R^7 represents a carboxy group or a tetrazol-5-yl group, and, where R^7 represents a carboxy group, salts of these compounds are also preferred. R^7 is preferably at the 2- or 3- position of the phenyl group, and more preferably at the 2-position.

The above compounds of the present invention necessarily contain at least one basic nitrogen atom in the imidazole ring and can therefore form acid addition salts. Examples of such acid addition salts include: addition salts with inorganic acids, such as hydrochloric acid, hydrobromic acid, sulfuric acid or phosphoric acid; and addition salts with organic acids such as maleic acid, fumaric acid, tartaric acid or citric acid.

Preferred classes of compounds of formula (I) (and salts and esters thereof) include:

R^1 represents an alkyl group having from 2 to 5 carbon atoms or an alkenyl group having from 3 to 5 carbon atoms;

R^2 and R^3 are independently selected from the group consisting of:
- hydrogen atoms,
- alkyl groups having from 1 to 4 carbon atoms,
- alkenyl groups having from 3 to 5 carbon atoms,
- cycloalkyl groups having 5 or 6 carbon atoms, benzyl, naphthyl and phenyl groups, and
- substituted benzyl and phenyl groups which are substituted by at least one substituent selected from the group consisting of substituents (b'), defined below;

substituents (b') are selected from the group consisting of methyl, ethyl, methoxy and ethoxy groups and fluorine and chlorine atoms;

R^4 represents:
- a hydrogen atom,
- an alkyl group having from 1 to 4 carbon atoms,
- an alkanoyl group having from 1 to 5 carbon atoms,
- a substituted alkanoyl group which has 2 or 3 carbon atoms and which is substituted by at least one substituent selected from the group consisting of fluorine and chlorine atoms and methoxy and ethoxy groups,
- an alkenoyl group having from 3 to 5 carbon atoms,
- a naphthoyl group,
- a benzoyl group,
- a substituted benzoyl group which is substituted by at least one substituent selected from the group consisting of substituents (b'), defined below, an alkoxycarbonyl group having from 2 to 5 carbon atoms,
- a tetrahydropyranyl, tetrahydrothiopyranyl, tetrahydrothienyl or tetrahydrofuryl group,
- a substituted tetrahydropyranyl, tetrahydrothiopyranyl, tetrahydrothienyl or tetrahydrofuryl group which is substituted by at least one substituent selected from the group consisting of chlorine and bromine atoms and methoxy groups,
- a group of formula —$SiR^aR^bR^c$, in which 1, 2 or 3 of the groups represented by R^a, R^b and R^c are independently selected from the group consisting of alkyl groups having from 1 to 4 carbon atoms, and 2, 1 or 0 of the groups represented by R^a, R^b and R^c are phenyl groups,
- a methoxymethyl, 2-methoxyethoxymethyl, 2,2,2-trichloroethoxymethyl, bis(2-chloroethoxy)methyl, benzyl, diphenylmethyl or naphthylmethyl group or a substituted benzyl group which is substituted by at least one substituent selected from the group consisting of substituents (b'), defined below, or a pivaloyloxymethoxycarbonyl group;

R^5 represents a group of formula —$COOR^{5a}$ or a group of formula —$CONR^8R^9$ in which:

R^{5a} represents
- a hydrogen atom,
- an alkyl group having from 1 to 4 carbon atoms,
- a phenyl, naphthyl, benzyl, diphenylmethyl or naphthylmethyl group,
- a substituted phenyl or benzyl group which is substituted by at least one substituent selected from the group consisting of substituents (b'), defined below,
- a group of formula —$SiR^aR^bR^c$, in which R^a, R^b and R^c are as defined above,

an alkanoyloxyalkyl group, in which the alkanoyl part has from 1 to 5 carbon atoms, and the alkyl part has from 1 to 4 carbon atoms,
a cycloalkanoyloxyalkyl group, in which the cycloalkanoyl part has 6 or 7 carbon atoms, and the alkyl part has from 1 to 4 carbon atoms,
an alkoxycarbonyloxyalkyl group, in which the alkoxy part has from 1 to 4 carbon atoms, and the alkyl part has from 1 to 4 carbon atoms,
a cycloalkoxycarbonyloxyalkyl group, in which the cycloalkoxy part has 5 or 6 carbon atoms, and the alkyl part has from 1 to 4 carbon atoms,
a [5-(phenyl- or alkyl-)-2-oxo-1,3-dioxolen-4-yl]-methyl group in which the alkyl part has from 1 to 4 carbon atoms, or
a phthalidyl group;

R^8 and R9 are independently selected from the group consisting of:
hydrogen atoms,
alkyl groups having from 1 to 4 carbon atoms, and substituted alkyl groups which have from 1 to 4 carbon atoms and which are substituted by at least one substituent selected from the group consisting of substituents (a'), defined below;
or R^8 and R^9 together represent an unsubstituted alkylene group which has 4 or 5 carbon atoms or a substituted alkylene group which has 4 or 5 carbon atoms and which is substituted by at least one substituent selected from the group consisting of carboxy groups, methoxycarbonyl groups and ethoxycarbonyl groups;

substituents (a') are selected from the group consisting of phenyl groups, furyl groups, thienyl groups, fluorine atoms, chlorine atoms, hydroxy groups, methoxy groups, ethoxy groups, carboxy groups and alkoxycarbonyl groups having from 2 to 5 carbon atoms;

R^6 represents a hydrogen atom, an alkyl group having from 1 to 4 carbon atoms, an alkoxy group having from 1 to 4 carbon atoms, a fluorine atom, a chlorine atom or a bromine atom;

R^7 represents a carboxy group or a tetrazol-5-yl group; and

the benzene ring which bears the substituents represented by R^6 and R^7 is at the 3- or 4- position of the benzyl group to which it is attached.

More preferred classes of compounds of formula (I) (and salts and esters) include:

R^1 represents an alkyl group having from 2 to 5 carbon atoms or an alkenyl group having from 3 to 5 carbon atoms;

R^2 and R^3 are independently selected from the group consisting of:
hydrogen atoms,
alkyl groups having from 1 to 4 carbon atoms,
alkenyl groups having from 3 to 5 carbon atoms,
cycloalkyl groups having 5 or 6 carbon atoms, and
benzyl and phenyl groups;

R^4 represents:
a hydrogen atom,
a methyl or ethyl group,
an alkanoyl group having from 1 to 5 carbon atoms,
an alkenoyl group having from 3 to 5 carbon atoms,
a benzoyl group, or
an alkoxycarbonyl group having from 2 to 5 carbon atoms;

R^{5a} represents a group of formula —$COOR^{5a}$ or a group of formula —$CONR^8R^9$ in which:

R^{5a} represents
a hydrogen atom,
an alkyl group having from 1 to 4 carbon atoms,
a benzyl group,
an alkanoyloxyalkyl group, in which the alkanoyl part has from 1 to 5 carbon atoms, and the alkyl part is a methyl or ethyl group,
a cycloalkanoyloxyalkyl group, in which the cycloalkanoyl part has 6 or 7 carbon atoms, and the alkyl part is a methyl or ethyl group,
an alkoxycarbonyloxyalkyl group, in which the alkoxy part has from 1 to 4 carbon atoms, and the alkyl part is a methyl or ethyl group,
a cycloalkoxycarbonyloxyalkyl group, in which the cycloalkoxy part has 5 or 6 carbon atoms, and the alkyl part is a methyl or ethyl group,
a [5-(phenyl-, methyl- or ethyl-)-2-oxo-1,3-dioxolen-4-yl]methyl group, or
a phthalidyl group;

R^8 and R^9 are independently selected from the group consisting of:
hydrogen atoms,
methyl groups,
ethyl groups, and
substituted methyl and ethyl groups which are substituted by at least one substituent selected from the group consisting of carboxy groups, methoxycarbonyl groups and ethoxycarbonyl groups;
or R^8 and R^9 together represent an unsubstituted alkylene group which has 4 or 5 carbon atoms or a substituted alkylene group which has 4 or 5 carbon atoms and which is substituted by at least one substituent selected from the group consisting of carboxy groups, methoxycarbonyl groups and ethoxycarbonyl groups;

R^6 represents a hydrogen atom, or it represents a methyl group, an ethyl group, a methoxy group, an ethoxy group, a fluorine atom or a chlorine atom on the 6-position of the benzene ring;

R^7 represents a carboxy group or a tetrazol-5-yl group at the 2- or 3- position of the benzene ring; and

the benzene ring which bears the substituents represented by R^6 and R^7 is at the 4-position of the benzyl group to which it is attached.

Still more preferred classes of compounds of formula (I) (and salts and esters thereof) include:

R^1 represents an alkyl group having from 2 to 5 carbon atoms;

R^2 and R^3 are independently selected from the group consisting of hydrogen atoms and alkyl groups having from 1 to 4 carbon atoms;

R^4 represents a hydrogen atom, a methyl group, an ethyl group or an alkanoyl group having from 1 to 5 carbon atoms;

R^5 represents a group of formula —$COOR^{5a}$ or a group of formula —$CONR^8R^9$, in which:
R^{5a} represents
a hydrogen atom,
a methyl, ethyl or benzyl group,
an alkanoyloxymethyl group, in which the alkanoyl part has from 1 to 5 carbon atoms,
a 1-(alkanoyloxy)ethyl group, in which the alkanoyl part has from 1 to 5 carbon atoms,
an alkoxycarbonyloxymethyl group, in which the alkoxy part has from 1 to 4 carbon atoms,
a 1-(alkoxycarbonyloxy)ethyl group, in which the alkoxy part has from 1 to 4 carbon atoms,

a [5-(phenyl- or methyl-)-2-oxo-1,3-dioxolen-4yl] methyl group, or
a phthalidyl group;

R^8 and R^9 are independently selected from the group consisting of hydrogen atoms, methyl groups, ethyl groups, methoxycarbonylmethyl groups, ethoxycarbonylmethyl groups and carboxymethyl groups; or R^8 and R^9 together represent a tetramethylene, pentamethylene, 1-carboxytetramethylene or 1-carboxypentamethylene group;

R^6 represents a hydrogen atom, or it represents a methyl group, an methoxy group, a fluorine atom or a chlorine atom at the 6-position of the benzene ring;

R^7 represents a carboxy group or a tetrazol-5-yl group at the 2-position of the benzene ring; and

the benzene ring which bears the substituents represented by R^6 and R^7 is at the 4-position of the benzyl group to which it is attached.

Even more preferred classes of compounds of formula (I) (including salts and esters thereof) include:

either

R^1 represents an ethyl, propyl or butyl group;

R^2 and R^3 are independently selected from the group consisting of hydrogen atoms and methyl groups;

R^4 represents a hydrogen atom or a methyl group;

R^5 represents a group of formula —$COOR^{5a}$, in which R^{5a} represents a hydrogen atom, a pivaloyloxymethyl group, an ethoxycarbonyloxymethyl group, a 1-(ethoxycarbonyloxy)ethyl group, an isopropoxycarbonyloxymethyl group, a 1-(isopropoxycarbonyloxy) ethyl group, a (5-methyl-2-oxo-1,3-dioxolen-4-yl)methyl group, or a phthalidyl group;

R^6 represents a hydrogen atom;

R^7 represents a carboxy group or a tetrazol-5-yl group at the 2-position of the benzene ring; and

the benzene ring which bears the substituents represented by R^6 and R^7 is at the 4-position of the benzyl group to which it is attached.

or

R^1 represents an ethyl, propyl or butyl group;

R^2 represents an isopropyl group or a t-butyl group;

R^3 represents a hydrogen atom;

R^4 represents a hydrogen atom or a methyl group;

R^5 represents a group of formula "$CONR^8R^9$, in which R^8 and R^9 are independently selected from the group consisting of hydrogen atoms, methyl groups, methoxycarbonylmethyl, ethoxycarbonylmethyl groups, and carboxymethyl groups;

R^6 represents a hydrogen atom;

R^7 represents a carboxy group or a tetrazol-5-yl group at the 2-position of the benzene ring; and

the benzene ring which bears the substituents represented by R^6 and R^7 is at the 4-position of the benzyl group to which it is attached.

The most preferred classes of compounds of formula (I) (and salts an esters thereof) include:

R^1 represents an ethyl, propyl or butyl group;

R^2 and R^3 both represent methyl groups;

R^4 represents a hydrogen atom or a methyl group;

R^5 represents a group of formula —$COOR^{5a}$ in which R^{5a} represents a hydrogen atom, a pivaloyloxymethyl group, an ethoxycarbonyloxymethyl group, a 1-(ethoxycarbonyloxy)ethyl group, an isopropoxycarbonyloxymethyl group, a 1-(isopropoxycarbonyloxy) ethyl group, a (5-methyl-2-oxo-1,3-dioxolen-4-yl)methyl group, or a phthalidyl group;

R^6 represents a hydrogen atom;

R^7 represents a carboxy group or a tetrazol-5-yl group at the 2-position of the benzene ring; and

the benzene ring which bears the substituents represented by R^6 and R^7 is at the 4-position of the benzyl group to which it is attached.

The compounds of the present invention may contain one or more asymmetric carbon atoms in their molecules, and can thus form optical isomers. Although these are all represented herein by a single molecular formula, the present invention includes both the individual, isolated isomers and mixtures, including racemates thereof. Where stereospecific synthesis techniques are employed or optically active compounds are employed as starting materials, individual isomers may be prepared directly; on the other hand, if a mixture of isomers is prepared, the individual isomers may be obtained by conventional resolution techniques.

Where R_p^1, R_p^3 or R_p^4 represents an alkyl group having from 1 to 6 carbon atoms, this may be a straight or branched chain group having from 1 to 6 carbon atoms, and examples include the methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, t-butyl, pentyl, isopentyl, neopentyl, t-pentyl, 2-methylbutyl, 1-ethylpropyl, 4-methylpentyl, 3-methylpentyl, 2-methylpentyl, 1-methylpentyl, 3,3-dimethylbutyl, 2,2-dimethylbutyl, 1,1-dimethylbutyl, 1,2-dimethylbutyl, 1,3-dimethylbutyl, 2,3-dimethylbutyl, 2-ethylbutyl, hexyl and isohexyl groups. Of these, we prefer those alkyl groups having from 1 to 4 carbon atoms, preferably the methyl, ethyl, propyl, isopropyl, butyl and isobutyl groups, more preferably the methyl and ethyl groups, and most preferably the methyl group.

Where R_p^1 represents a cycloalkyl group, this has from 3 to 6 ring carbon atoms, and examples include the cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl groups, preferably the cyclopropyl group.

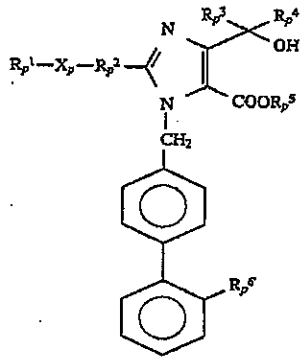
Where R^p represents an alkanoyl group having from 1 to 6 carbon atoms, this may be a straight or branched chain group having from 1 to 6 carbon atoms, and examples include the formyl, acetyl, propionyl, butyryl, isobutyryl, pivaloyl, valeryl, isovaleryl and hexanoyl groups, of which we prefer the acetyl and propionyl groups, most preferably the acetyl group.

Where R_p^2 represents an alkylene or alkylidene group, this is a bivalent saturated aliphatic hydrocarbon group having from 1 to 4 carbon atoms. Where the two "free" valencies are on the same carbon atom, the group is generally referred to as an "alkylidene" group; where they are on different carbon atoms, it is commonly referred to as an "alkylene" group. The term "alkylene" is also often used to embrace both types of group. Examples of such groups include the methylene, ethylene, trimethylene, propylene, ethylethylene, tetramethylene, ethylidene, propylidene, butylidene and isobutylidene groups, of which those groups having 1 or 2 carbon atoms are preferred, particularly the methylene group.

The compounds of formula $(I)_p$ of the present invention contain a carboxy group at the 5-position of the imidazole group and may contain another carboxy group if this is the meaning of R_p^6. These groups can of course, form esters. There is no particular restriction on the nature of the ester group, provided that, where the compound is intended for therapeutic purposes, it is pharmaceutically acceptable (i.e., it is not less active, or unacceptably less active than the free acid, and it is not more toxic, or unacceptably more toxic,

than the free acid). Where, however, the compound is intended for non-therapeutic purposes, for example as an intermediate in the preparation of other, and possibly more active, compounds, even this restriction does not apply. In general, however, any protecting group commonly used in the field of synthetic organic chemistry or any ester group capable of conversion to a carboxy group under physiological conditions, to form a pro-drug, may be used.

The compounds of formula $(I)_p$ and their esters may collectively be represented by the formula $(Ia)_p$:



$(Ia)_p$

(in which: R_p^1, R_p^2, R_p^3, R_p^4 and X_p are as defined above; R_p^5 represents a hydrogen atom or an ester group; and R_p^6 represents a carboxy group, an esterified carboxy group or a tetrazol-5-yl group).

Examples of such ester groups which may be represented by R_p^5 or may be included in the esterified carboxy group represented by R^{p6} include:

alkyl groups having from 1 to 6 carbon atoms, such as those exemplified above in relation to R_p^1 etc.;

haloalkyl groups having from 1 to 6 carbon atoms, such as the fluoromethyl, trifluoromethyl, trichloromethyl, 2,2,2-trifluoroethyl, 2,2,2-trichloroethyl, 2-fluoroethyl, 2-chloroethyl, 2-iodoethyl, 3-chloro- propyl, 4-fluorobutyl and 6-iodohexyl groups, of which we prefer the 2,2,2-trichloroethyl and 2-chloroethyl groups;

hydroxyalkyl groups having from 1 to 6 carbon atoms and having at least one, and preferably 1 or 2, hydroxy groups, such as the 2-hydroxyethyl, 2,3-dihydroxypropyl, 3-hydroxypropyl, 3,4-dihydroxybutyl and 4-hydroxybutyl groups, of which we prefer the 2-hydroxyethyl group;

alkoxyalkyl and alkoxyalkoxyalkyl groups, in which the or each alkoxy part has from 1 to 6 carbon atoms and the alkyl part has from 1 to 6 carbon atom, for example the methoxymethyl, 2-methoxyethyl, 2-ethoxyethyl, 3-methoxypropyl, 4-methoxybutyl, propoxymethyl, butoxymethyl and 2-methoxyethoxymethyl groups, of which we prefer the methoxymethyl group;

the phenacyl group;

alkoxycarbonylalkyl groups, in which the alkoxy part has from 1 to 8 carbon atoms and the alkyl part has from 1 to 6 carbon atoms, such as the methoxycarbonylmethyl, ethoxycarbonylmethyl, propoxycarbonylmethyl, isopropoxycarbonylmethyl, butoxycarbonylmethyl, t-butoxycarbonylmethyl, pentyloxycarbonylmethyl, hexyloxycarbonylmethyl, heptyloxycarbonylmethyl, octyloxycarbonylmethyl, 2-methoxycarbonylethyl, 2-ethoxycarbonylethyl, 2-propoxycarbonylethyl, 2-isopropoxycarbonylethyl, 2-butoxycarbonylethyl, 2-t-butoxycarbonylethyl, 2-pentyloxycarbonylethyl, 2-hexyloxycarbonylethyl, 2-heptyloxycarbonylethyl, 2-octyloxycarbonylethyl, 3-methoxycarbonylpropyl, 3-ethoxycarbonylpropyl, 4-methoxycarbonylbutyl, 4-ethoxycarbonylbutyl, 5-methoxycarbonylpentyl, 5-ethoxycarbonylpentyl, 6-methoxycarbonylhexyl and 6-ethoxycarbonylhexyl groups, of which the methoxycarbonylmethyl group is preferred;

cyanoalkyl groups, in which the alkyl part has from 1 to 6 carbon atoms, such as the cyanomethyl, 2-cyanoethyl, 3-cyanopropyl, 4-cyanobutyl, 5-cyanopentyl and 6-cyanohexyl groups, of which the cyanomethyl and 2-cyanoethyl groups are preferred;

alkylthiomethyl groups, in which the alkyl part has from 1 to 6 carbon atoms, such as the methylthiomethyl, ethylthiomethyl, propylthiomethyl, butylthiomethyl, pentylthiomethyl and hexylthiomethyl groups, of which the methylthiomethyl and ethylthiomethyl groups are preferred;

arylthiomethyl groups, in which the aryl part is a carbocyclic aromatic ring having from 6 to 10 ring carbon atoms and is unsubstituted or substituted, preferably unsubstituted, for example the phenylthiomethyl and naphthylthiomethyl groups; alkanesulfonylalkyl groups, in which each alkyl part (which may be the same as each other or different from each other) has from 1 to 6 carbon atoms and in which the alkane part is unsubstituted or substituted by at least one halogen atom, for example the 2-methanesulfonylethyl and 2-trifluoromethanesulfonylethyl groups;

arylsulfonylalkyl groups, in which the aryl part has from 6 to 10 ring carbon atoms and the alkyl part has from 1 to 6 carbon atoms, and where the aryl part is unsubstituted or is substituted, preferably by at least one alkyl group, for example the 2-benzenesulfonylethyl, 2-(1-naphthalenesulfonyl)ethyl, 2-p-toluenesulfonylethyl, 3-benzenesulfonylpropyl, 3-(1-naphthalenesulfonyl)propyl, 3-p-toluenesulfonylpropyl, 6-benzenesulfonylhexyl, 6-(1-naphthalenesulfonyl) hexyl, 6-p-toluenesulfonylhexyl, benzenesulfonylmethyl and p-toluenesulfonylmethyl groups, and preferably the 2-benzenesulfonylethyl and 2-p-toluenesulfonylethyl groups;

aralkyl groups, in which an alkyl group having from 1 to 6 carbon atoms is substituted by at least one (and preferably from 1 to 3) aryl groups which have from 6 to 10 ring carbon atoms and which are unsubstituted or are substituted, preferably unsubstituted; examples include the benzyl, diphenylmethyl, triphenylmethyl, 1-naphthylmethyl, 2-naphthylmethyl, phenethyl, 1-phenylethyl, 3-phenylpropyl, 2-phenylpropyl, 1-phenylpropyl, 4-phenylbutyl, 5-phenylpentyl and 6-phenylhexyl groups, of which the benzyl, diphenylmethyl and 1-naphthylmethyl groups are preferred and the benzyl group is most preferred;

aryl groups having from 6 to 10, preferably 6 or 10, ring carbon atoms, which may be unsubstituted or substituted (preferably unsubstituted), for example the phenyl and naphthyl groups, of which the phenyl group is preferred;

alkanoyloxyalkyl groups, in which the alkanoyl and alkyl parts both have from 1 to 6 carbon atoms, for example the formyloxymethyl, acetoxymethyl, propionyloxymethyl, butyryloxymethyl, pivaloyloxymethyl, valeryloxymethyl, isovaleryloxymethyl, hexanoyloxymethyl, 1-formyloxyethyl, 1-acetoxyethyl, 1-propionyloxyethyl, 1-butyryloxyethyl, 1-pivaloyloxyethyl, 1-valery-

loxyethyl, 1-isovaleryloxyethyl, 1-hexanoyloxyethyl, 2-formyloxyethyl, 2-acetoxyethyl, 2-propionyloxyethyl, 2-butyryloxyethyl, 2-pivaloyloxyethyl, 2-valeryloxyethyl, 2-isovaleryloxyethyl, 2-hexanoyloxyethyl, 1-formyloxypropyl, 1-acetoxypropyl, 1-propionyloxypropyl, 1-butyryloxypropyl, 1-pivaloyloxypropyl, 1-valeryoxypropyl, 1-isovaleryloxypropyl, 1-hexanonyloxypropyl, 1-acetoxybutyl, 1-propionyloxybutyl, 1-butyryloxybutyl, 1-pivaloyloxybutyl, 1-acetoxypentyl, 1-propionyloxypentyl, 1-butyryloxypentyl, 1-pivaloyloxypentyl and 1-pivaloyloxyhexyl groups, of which we prefer the formyloxymethyl, acetoxymethyl, propionyloxymethyl, butyryloxymethyl, pivaloyloxymethyl, 1-formyloxyethyl, 1-acetoxyethyl, 1-propionyloxyethyl, 1-butyryloxyethyl and 1-pivaloyloxyethyl groups and more prefer the acetoxymethyl, propionyloxymethyl, butyryloxymethyl, pivaloyloxymethyl, 1-acetoxyethyl, 1-propionyloxyethyl, 1-butyryloxyethyl and 1-pivaloyloxyethyl groups, the pivaloyloxymethyl and 1-pivaloyloxyethyl groups being most preferred;

cycloalkanecarbonyloxyalkyl groups, in which the cycloalkane part has 5 or 6 ring carbon atoms and the alkyl part has from 1 to 6 carbon atoms, for example the cyclopentanecarbonyloxymethyl, cyclohexanecarbonyloxymethyl, 1-cyclopentanecarbonyloxyethyl, 1-cyclohexanecarbonyloxyethyl, 1-cyclopentanecarbonyloxypropyl, 1-cyclohexanecarbonyloxypropyl, 1-cyclopentanecarbonyloxybutyl and 1-cyclohexanecarbonyloxybutyl groups, preferably the cyclopentanecarbonyloxymethyl, cyclohexanecarbonyloxymethyl, 1-cyclopentanecarbonyloxyethyl and 1-cyclohexanecarbonyloxyethyl groups;

alkoxycarbonyloxyalkyl groups, in which the alkoxy and alkyl parts both have from 1 to 6 carbon atoms, for example the methoxycarbonyloxymethyl, ethoxycarbonyloxymethyl, propoxycarbonyloxymethyl, isopropoxycarbonyloxymethyl, butoxycarbonyloxymethyl, isobutoxycarbonyloxymethyl, pentyloxycarbonyloxymethyl, hexyloxycarbonyloxymethyl, 1-methoxycarbonyloxyethyl, 1-ethoxycarbonyloxyethyl, 1-propoxycarbonyloxyethyl, 1-isopropoxycarbonyloxyethyl, 1-butoxycarbonyloxyethyl, 1-isobutoxycarbonyloxyethyl, 1-pentyloxycarbonyloxyethyl, 1-hexyloxycarbonyloxyethyl, 2-methoxycarbonyloxyethyl, 2-ethoxycarbonyloxyethyl, 2-propoxycarbonyloxyethyl, 2-isopropoxycarbonyloxyethyl, 2-butoxycarbonyloxyethyl, 2-isobutoxycarbonyloxyethyl, 2-pentyloxycarbonyloxyethyl, 2-hexyloxycarbonyloxyethyl, 1-methoxycarbonyloxypropyl, 1-ethoxycarbonyloxypropyl, 1-propoxycarbonyloxypropyl, 1-isopropoxycarbonyloxypropyl, 1-butoxycarbonyloxypropyl, 1-isobutoxycarbonyloxypropyl, 1-pentyloxycarbonyloxypropyl, 1-hexyloxycarbonyloxypropyl, 1-methoxycarbonyloxybutyl, 1-ethoxycarbonyloxybutyl, 1-propoxycarbonyloxybutyl, 1-isopropoxycarbonyloxybutyl, 1-butoxycarbonyloxybutyl, 1-isobutoxycarbonyloxybutyl, 1-methoxycarbonyloxypentyl, 1-ethoxycarbonyloxypentyl, 1-methoxycarbonyloxyhexyl and 1-ethoxycarbonyloxyhexyl groups, of which we prefer the methoxycarbonyloxymethyl, ethoxycarbonyloxymethyl, propoxycarbonyloxymethyl, isopropoxycarbonyloxymethyl, butoxycarbonyloxymethyl, isobutoxycarbonyloxymethyl, 1-methoxycarbonyloxyethyl, 1-ethoxycarbonyloxyethyl, 1-propoxycarbonyloxyethyl, 1-isopropoxycarbonyloxyethyl, 1-butoxycarbonyloxypropyl, 1-isobutoxycarbonyloxypropyl, 1-methoxycarbonyloxypropyl, 1-ethoxycarbonyloxypropyl, 1-propoxycarbonyloxypropyl, 1-isopropoxycarbonyloxypropyl, 1-butoxycarbonyloxypropyl, 1-isobutoxycarbonyloxypropyl, 1-methoxycarbonyloxybutyl, 1-ethoxycarbonyloxybutyl, 1-propoxycarbonyloxybutyl, 1-isopropoxycarbonyloxybutyl, 1-butoxycarbonyloxybutyl and 1-isobutoxycarbonyloxybutyl groups, and more prefer the methoxycarbonyloxymethyl, ethoxycarbonyloxymethyl, propoxycarbonyloxymethyl, isopropoxycarbonyloxymethyl, butoxycarbonyloxymethyl, isobutoxycarbonyloxymethyl, 1-methoxycarbonyloxyethyl, 1-ethoxycarbonyloxyethyl, 1-propoxycarbonyloxyethyl, 1-isopropoxycarbonyloxyethyl, 1-butoxycarbonyloxyethyl and 1-isobutoxycarbonyloxyethyl groups, the methoxycarbonyloxymethyl, ethoxycarbonyloxymethyl, isopropoxycarbonyloxymethyl, 1-methoxycarbonyloxyethyl, 1-ethoxycarbonyloxyethyl and 1-isopropoxycarbonyloxyethyl groups being most preferred;

cycloalkyloxycarbonyloxyalkyl groups, in which the cycloalkyl part has 5 or 6 ring carbon atoms and the alkyl part has from 1 to 6 carbon atoms, for example the cyclopentyloxycarbonyloxymethyl, cyclohexyloxycarbonyloxymethyl, 1-cyclopentyloxycarbonyloxyethyl, 1-cyclohexyloxycarbonyloxyethyl, 1-cyclopentyloxycarbonyloxypropyl, 1-cyclohexyloxycarbonyloxypropyl, 1-cyclopentyloxycarbonyloxybutyl and 1-cyclohexyloxycarbonyloxybutyl groups, of which we prefer the cyclopentyloxycarbonyloxymethyl, cyclohexyloxycarbonyloxymethyl, 1-cyclopentyloxycarbonyloxyethyl and 1-cyclohexyloxycarbonyloxyethyl groups;

[5-(aryl or alkyl)-2-oxo-1,3-dioxolen-4-yl]methyl groups, in which the aryl group is a carbocyclic aromatic group having from 6 to 10, preferably 6 or 10, ring carbon atoms (and is substituted, preferably with a halogen atom, an alkyl group or an alkoxy group, or unsubstituted, preferably unsubstituted), and the alkyl group has from 1 to 6 carbon atoms, for example the (5-phenyl-2-oxo-1,3-dioxolen-4-yl)methyl, [5-(4-methylphenyl)-2-oxo-1,3-dioxolen-4-yl]methyl, [5-(4-methoxyphenyl)-2-oxo-1,3-dioxolen-4-yl]methyl, [5-(4-fluorophenyl)-2-oxo-1,3-dioxolen-4-yl]methyl, [5-(4-chlorophenyl)-2-oxo-1,3-dioxolen-4-yl]methyl, (5-methyl-2-oxo-1,3-dioxolen-4-yl)methyl, (5-ethyl-2-oxo-1,3-dioxolen-4-yl)methyl, (5-propyl-2-oxo-1,3-dioxolen-4-yl)methyl, (5-isopropyl-2-oxo-1,3 -dioxolen-4-yl)methyl and (5-butyl-2-oxo-1,3-dioxolen-4-yl)methyl groups, of which we prefer the (5-phenyl-2-oxo-1,3-dioxolen-4-yl)methyl, (5-methyl-2-oxo-1,3-dioxolen-4-yl)methyl and (5-ethyl-2-oxo-1,3-dioxolen-4-yl)methyl groups, and more prefer the (5-methyl-2-oxo-1,3-dioxolen-4-yl)methyl group; and

the phthalidyl group.

In the above groups for formula $(I)_p$, where an aryl group is referred to as substituted, examples of suitable substituents include:

alkyl groups having from 1 to 6 carbon atoms, such as those exemplified above in relation to R_p^1 etc.;

alkoxy groups having from 1 to 6 carbon atoms, such as the methoxy, ethoxy, propoxy, isopropoxy, t-butoxy, pentyloxy and hexyloxy groups;

halogen atoms, such as the fluorine, chlorine, bromine and iodine atoms;

preferably alkyl groups having from 1 to 4 carbon atoms, alkoxy groups having from 1 to 4 carbon atoms, and florine,

chlorine or bromine atoms, most preferably a methyl, ethyl, methoxy or ethoxy group, or a fluorine or chlorine atom.

Examples of such preferred ester groups for formula $(I)_p$ include:

- alkyl groups having from 1 to 4 carbon atoms;
- phenyl groups which are unsubstituted or are substituted by at least one substituent selected from the group consisting of methyl groups, ethyl groups, methoxy groups, ethoxy groups, fluorine atoms and chlorine atoms;
- naphthyl groups;
- benzyl groups which are unsubstituted or are substituted by at least one substituent selected from the group consisting of methyl groups, ethyl groups, methoxy groups, ethoxy groups, fluorine atoms and chlorine atoms;
- diphenylmethyl groups;
- naphthylmethyl groups;
- alkanoyloxyalkyl groups in which the alkanoyl part has from 1 to 5 carbon atoms and the alkyl part has from 1 to 4 carbon atoms;
- cycloalkanecarbonyloxyalkyl groups in which the cycloalkane part has 5 or 6 ring carbon atoms and the alkyl part has from 1 to 4 carbon atoms;
- alkoxycarbonyloxyalkyl groups in which the alkoxy and alkyl parts both have from 1 to 4 carbon atoms;
- cycloalkyloxycarbonyloxyalkyl groups in which the cycloalkyl part has 5 or 6 ring carbon atoms and the alkyl part has from 1 to 4 carbon atoms;
- [5-phenyl- or 5-alkyl-2-oxo-1,3-dioxolen-4-yl]methyl groups in which the alkyl part has from 1 to 4 carbon atoms; and
- the phthalidyl group.

Still more preferred ester groups for formula $(I)_p$ include:

- alkyl groups having from 1 to 4 carbon atoms;
- the benzyl group;
- alkanoyloxyalkyl groups in which the alkanoyl part has from 1 to 5 carbon atoms and the alkyl part has 1 or 2 carbon atoms;
- cycloalkanecarbonyloxyalkyl groups in which the cycloalkane part has 5 or 6 ring carbon atoms and the alkyl part has 1 or 2 carbon atoms;
- alkoxycarbonyloxyalkyl groups in which the alkoxy part has from 1 to 4 carbon atoms and the alkyl part has 1 or 2 carbon atoms;
- cycloalkyloxycarbonyloxyalkyl groups in which the cycloalkane part has 5 or 6 ring carbon atoms and the alkyl part has 1 or 2 carbon atoms;
- [5-phenyl-, 5-methyl- or 5-ethyl-2-oxo-1,3-dioxolene-4-yl]methyl groups; and
- the phthalidyl group.

The most preferred ester groups for formula $(I)_p$ include the pivaloyloxymethyl, ethoxycarbonyloxymethyl, 1-(ethoxycarbonyloxy)ethyl, isopropoxycarbonyloxymethyl, 1-(isopropoxycarbonyloxy)ethyl, (5-methyl-2-oxo-1,3-dioxolen-4-yl)methyl and phthalidyl groups.

Preferred compounds of formula $(I)_p$ or $(Ia)_p$ (and salts and (where appropriate) esters thereof) include:

(A) R_p^1 represents a hydrogen atom, a methyl group, an ethyl group, a cyclopropyl group or an acetyl group, particularly a methyl or ethyl group;

(B) R_p^2 represents a single bond, a methylene group, an ethylene group or an ethylidene group;

(C) R_p^3 and R_p^4 are the same or different and each represents a hydrogen atom, a methyl group or an ethyl group, particularly a methyl or ethyl group;

(D) R_p^5 represents

- a hydrogen atom,
- an alkyl group having from 1 to 4 carbon atoms,
- a phenyl group,
- a phenyl group substituted by at least one substituent selected from the group consisting of methyl groups, ethyl groups, methoxy groups, ethoxy groups, fluorine atoms and chlorine atoms,
- a naphthyl group,
- a benzyl group,
- a benzyl group substituted by at least one substituent selected from the group consisting of methyl groups, ethyl groups, methoxy groups, ethoxy groups, fluorine atoms and chlorine atoms,
- a diphenylmethyl group,
- a naphthylmethyl group,
- an alkanoyloxyalkyl group in which the alkanoyl part has from 1 to 5 carbon atoms and the alkyl part has from 1 to 4 carbon atoms,
- a cycloalkanecarbonyloxyalkyl group in which the cycloalkane part has 5 or 6 carbon atoms and the alkyl part has from 1 to 4 carbon atoms,
- an alkoxycarbonyloxyalkyl group in which the alkoxy and alkyl parts each have from 1 to 4 carbon atoms,
- a cycloalkyloxycarbonyloxyalkyl group in which the cycloalkyl part has 5 or 6 carbon atoms and the alkyl part has from 1 to 4 carbon atoms, a (5-phenyl-2-oxo-1,3-dioxolen-4-yl)methyl group, a (5-alkyl-2-oxo-1,3-dioxolen-4-yl)methyl group, in which the alkyl part has from 1 to 4 carbon atoms, or
- a phthalidyl group;

(E) R_p^6 represents a carboxy group or a tetrazol-5-yl group.

Of formulas $(I)_p$ and $(Ia)_p$, we particularly prefer those compounds of formula $(Ia)_p$ and salts and esters thereof in which R_p^1 is as defined in (A) above, R_p^2 is as defined in (B) above, R_p^3 and R_p^4 are as defined in (C) above, R_p^5 is as defined in (D) above and R_p^6 is as defined in (E) above.

More preferred compounds of the present invention are those compounds of formula $(I)_p$ or $(Ia)_p$ and salts and (where appropriate) esters thereof, in which:

(F) the group of formula $R_p^1—X_p—R_p^2—$ represents a methoxymethyl group, an ethoxymethyl group, a 1-methoxyethyl group, a 2-methoxyethyl group, a 2-ethoxyethyl group, a methylthiomethyl group, an ethylthiomethyl group, a 1-methylthioethyl group, 2-methylthioethyl, a 2-ethylthioethyl group, a methylthio group or an ethylthio group;

(G) R_p^3 and R_p^4 are the same or different and each represents a methyl or ethyl group;

(H) R_p^5 represents a hydrogen atom, an alkyl group having from 1 to 4 carbon atoms, a benzyl group, an alkanoyloxyalkyl group in which the alkanoyl part has from 1 to 5 carbon atoms and the alkyl part has 1 or 2 carbon atoms, a cycloalkanecarbonyloxyalkyl group in which the cycloalkane part has 5 or 6 carbon atoms and the alkyl part has 1 or 2 carbon atoms, an alkoxycarbonyloxyalkyl group in which the alkoxy part has from 1 to 4 carbon atoms and the alkyl part has 1 or 2 carbon atoms, a cycloalkyloxycarbonyloxyalkyl group in which the cycloalkyl part has 5 or 6 carbon atoms and the alkyl part has 1 or 2 carbon atoms, a (5-phenyl-, 5-methyl- or 5-ethyl- 2-oxo-1,3-dioxolen-4-yl)methyl group, or a phthalidyl group.

Particularly preferred compounds are of formula $(Ia)_p$ and salts and esters thereof in which R_p^1—X_p—R_p^2 is as defined in (F) above, R_p^3 and R_p^4 are as defined in (G) above, R_p^5 is as defined in (H) above and $R_p^{6'}$ is as defined in (E) above.

The most preferred compounds of formula $(I)_p$ or $(Ia)_p$ and salts and (where appropriate) esters thereof, are in which:

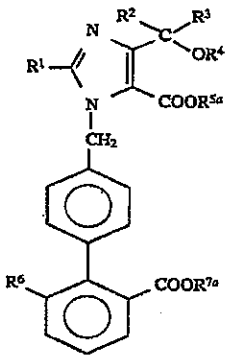
(I) the group of formula R_p^1—X_p—R_p^2— represents a methoxymethyl group, an ethoxymethyl group, a methylthiomethyl group, a methylthio group or an ethylthio group;

(J) R_p^3 and R_p^4 both represent methyl groups; and

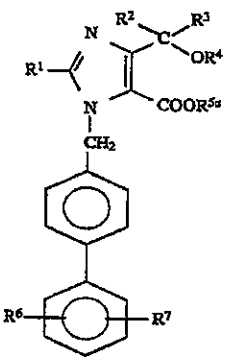
(K) R_p^5 represents a hydrogen atom, a pivaloyloxymethyl group, an ethoxycarbonyloxymethyl group, a 1-(ethoxycarbonyloxy)ethyl group, an isopropoxycarbonyloxymethyl group, a 1-(isopropoxycarbonyloxy) ethyl group, a (5-methyl-2-oxo-1,3-dioxolen-4yl)methyl group or a phthalidyl group.

Particularly preferred compounds of formula $(Ia)_p$ and salts and esters thereof are in which R_p^1—X_p—R_p^2 is as defined in (I) above, R_p^3 and R_p^4 are as defined in (J) above, R_p^5 is as defined in (K) above and $R_p^{6'}$ is as defined in (E) above.

Specific examples of individual compounds of the present invention are shown in the following formulae (I-1), (I-2), (I-3), (I-4), (I-5)and (I-6):



(I-1)



(I-2)

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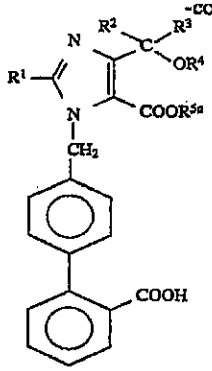
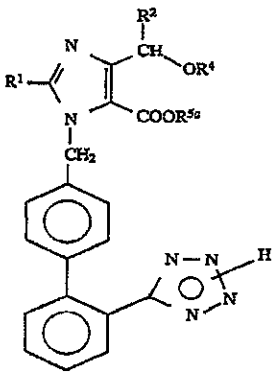
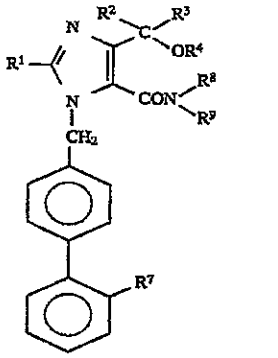


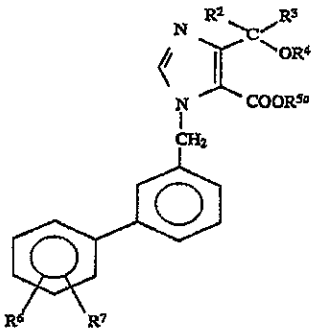
(I-3)



(I-4)



(I-5)



(I-6)

In these formulae, the meanings of the various substituent groups are as given in the following Tables 1 to 6, in which Table 1 relates to formula (I-1), Table 2 relates to formula

(I-2), Table 3 relates to formula (I-3), and so on. In the Tables, the following abbreviations are used:

Ac	acetyl
Boz	benzoyl
Bu	butyl
iBu	isobutyl
tBu	t-butyl
Buc	butoxycarbonyl
iBuc	isobutoxycarbonyl
Bz	benzyl
Et	ethyl
Etc	ethoxycarbonyl
Fo	formyl
Fu	2-furyl
cHx	cyclohexyl
Im	4-imidazolyl

-continued

Me	methyl
Mec	methoxycarbonyl
Mod	(5-methyl-2-oxo-1,3-dioxolen-4-yl)methyl
Ph	phenyl
Phth	phthalidyl
Piv	pivaloyl
Pn	pentyl
cPn	cyclopentyl
iPn	isopentyl
Pr	propyl
iPr	isopropyl
iPrc	isopropoxycarbonyl
Prn	propionyl
Tz	tetrazol-5-yl
Th	2-thienyl

TABLE 1

Cpd. No.	R^1	R^2	R^3	R^4	R^{5a}	R^6	R^{7a}
1-1	Pr	H	H	H	H	H	H
1-2	Bu	H	H	H	H	H	H
1-3	—CH═CH—Et	N	B	H	H	H	H
1-4	Pn	H	H	H	H	H	H
1-5	Bu	H	H	H	Me	H	H
1-6	Bu	H	H	H	Et	H	H
1-7	Bu	H	H	H	Bu	H	H
1-8	Bu	H	H	H	Bz	H	H
1-9	Bu	H	H	Me	H	H	H
1-10	Bu	H	H	Et	H	H	H
1-11	Bu	H	H	Fo	H	H	H
1-12	Bu	H	H	Ac	H	H	H
1-13	Bu	H	H	Boz	H	H	H
1-14	Bu	H	H	Me	Et	H	H
1-15	Bu	H	H	Me	$PivOCH_2$—	H	H
1-16	Bu	H	H	H	H	Cl	H
1-17	Bu	H	H	H	Et	Cl	H
1-18	Bu	H	H	H	H	OMe	H
1-19	Bu	H	H	H	Et	OMe	H
1-20	Bu	H	H	H	H	OEt	H
1-21	Bu	H	H	H	Et	OEt	H
1-22	Bu	H	H	H	Mod	H	H
1-23	Bu	H	H	H	$EtcOCH_2$—	H	H
1-24	Bu	H	H	H	1-(EtcO)Et	H	H
1-25	Bu	Me	H	H	H	H	H
1-26	Bu	Me	H	H	Et	H	H
1-27	Bu	Me	H	H	$PivOCH_2$—	H	H
1-28	Bu	Me	H	H	Mod	H	H
1-29	Bu	Me	H	Ac	H	H	H
1-30	Bu	Me	H	Ac	Et	H	H
1-31	Bu	Me	Me	H	H	H	H
1-32	Bu	Me	Me	H	Et	H	H
1-33	Bu	Me	Me	H	Bu	H	H
1-34	Bu	Me	Me	H	Me	H	H
1-35	Bu	Me	Me	H	$PivOCH_2$—	H	H
1-36	Bu	Me	Me	H	Mod	H	H
1-37	Bu	Me	Me	Me	H	H	H
1-38	Bu	Me	Me	Me	Et	H	H
1-39	Bu	Me	Me	Fo	H	H	H
1-40	Bu	Me	Me	Fo	Et	H	H
1-41	Bu	Me	Me	Ac	H	H	H
1-42	Bu	Me	Me	Ac	Et	H	H
1-43	Bu	Me	Me	Boz	H	H	H
1-44	Bu	Me	Me	Boz	Et	H	H
1-45	Bu	Me	Me	H	H	Cl	H
1-46	Bu	Me	Me	H	Et	Cl	H
1-47	Bu	Me	Me	H	H	OMe	H
1-48	Bu	Me	Me	H	Et	OMe	H
1-49	Pr	Me	Me	H	H	H	H
1-50	Pr	Me	Me	H	Et	H	H
1-51	Pr	Me	Me	Ac	Et	H	H
1-52	Pr	Me	Me	H	H	OMe	H
1-53	Pr	Me	Me	H	Et	OMe	H
1-54	Pn	Me	Me	H	H	H	H
1-55	Pn	Me	Me	H	Et	H	H

TABLE 1-continued

Cpd. No.	R^1	R^2	R^3	R^4	R^{5a}	R^6	R^{7a}
1-56	Et	Me	H	H	H	H	H
1-57	Et	Me	H	H	Et	H	H
1-58	Et	Me	H	H	$PivOCH_2$—	H	H
1-59	Et	Me	H	H	Mod	H	H
1-60	Et	Me	H	H	$EtcOCH_2$—	H	H
1-61	Et	Me	H	H	1-(EtcO)Et	H	H
1-62	Bu	Et	H	H	H	H	H
1-63	Bu	Et	H	H	Et	H	H
1-64	Bu	Et	H	H	H	Cl	H
1-65	Bu	Et	H	H	Et	Cl	H
1-66	Bu	Et	H	H	H	OMe	H
1-67	Bu	Et	H	H	Et	OMe	H
1-68	Bu	iPr	H	H	H	H	H
1-69	Bu	iPr	H	H	Et	H	H
1-70	Bu	iPr	H	H	H	Cl	H
1-71	Bu	iPr	H	H	Et	Cl	H
1-72	Bu	iPr	H	H	H	OMe	H
1-73	Bu	iPr	H	H	Et	OMe	H
1-74	Bu	tBu	H	H	H	H	
1-75	Bu	tBu	H	H	Et	H	H
1-76	Bu	tBu	H	H	H	Cl	H
1-77	Bu	tBu	H	H	Et	Cl	H
1-78	Bu	tBu	H	H	H	OMe	H
1-79	Bu	tBu	H	H	Et	OMe	H
1-80	Bu	Ph	H	H	H	H	H
1-81	Bu	Ph	H	H	Et	H	H
1-82	Bu	Et	Me	H	H	H	H
1-83	Bu	Et	Me	H	Et	H	H
1-84	Bu	Et	Et	H	H	H	H
1-85	Bu	Et	Et	H	Et	H	H
1-86	Bu	Et	Et	H	H	Cl	H
1-87	Bu	Et	Et	H	Et	Cl	H
1-88	Bu	Et	Et	N	H	OMe	H
1-89	Bu	Et	Et	H	Et	OMe	H
1-90	Bu	Pr	H	H	H	H	H
1-91	Bu	Pr	H	H	Et	H	H
1-92	Pr	Pr	H	H	H	H	H
1-93	Pr	Pr	H	H	Et	H	H
1-94	Bu	H	H	H	Me	H	tBu
1-95	Bu	H	H	H	Et	H	tBu
1-96	Bu	H	H	H	H	H	tBu
1-97	Bu	H	H	H	$PivOCH_2$—	H	tBu
1-98	Bu	H	H	H	$PivOCH_2$—	H	H
1-99	Bu	H	H	Me	Me	H	tBu
1-100	Pr	H	H	H	Et	H	H
1-101	Pr	H	H	H	Bu	H	H
1-102	Pr	H	H	H	$PivOCH_2$—	H	H
1-103	Pr	H	H	H	Mod	H	H
1-104	Pr	H	H	H	H	Cl	H
1-105	Pr	H	H	H	Et	Cl	H
1-106	Pr	H	H	H	H	OMe	H
1-107	Pr	H	H	H	Et	OMe	H
1-108	Pr	Me	Me	H	H	Cl	H
1-109	Pr	Me	Me	H	Et	Cl	H
1-110	Pr	Me	Me	H	H	H	Et
1-111	Pr	Me	Me	H	H	H	Bu
1-112	Pr	Me	Me	H	H	H	$PivOCH_2$—
1-113	Bu	Me	Me	H	H	H	Et
1-114	Bu	Me	Me	H	H	H	Bu
1-115	Bu	Me	Me	H	H	H	$PivOCH_2$—
1-116	Bu	Me	Me	Mcc	H	H	H
1-117	Bu	Me	Me	Etc	H	H	H
1-118	Bu	Me	Me	H	Et	H	tBu
1-119	Pr	Me	Me	H	Et	H	tBu
1-120	Bu	Me	Me	H	H	F	H
1-121	Bu	H	H	Me	Me	H	H
1-122	Bu	Me	Me	H	H	Cl	tBu
1-123	Bu	Me	Me	H	Et	Cl	tBu
1-124	Bu	Me	Me	H	H	OMe	tBu
1-125	Bu	Me	Me	H	Et	OMe	tBu
1-126	Pr	Me	Me	H	H	Cl	tBu
1-127	Pr	Me	Me	H	Et	Cl	tBu
1-128	Pr	Me	Me	H	H	OMe	tBu
1-129	Pr	Me	Me	H	Et	OMe	tBu
1-130	Et	Me	Me	H	Et	H	tBu
1-131	Et	Me	Me	H	Et	H	H

TABLE 1-continued

Cpd. No.	R^1	R^2	R^3	R^4	R^{5a}	R^6	R^{7a}
1-132	Et	Me	Me	H	H	H	H
1-133	Pr	Me	H	H	$PivOCH_2$—	H	H
1-134	Pr	Me	H	H	Mod	H	H
1-135	Pr	Me	H	H	$EtcOCH_2$—	H	H
1-136	Pr	Me	H	H	1-(EtcO)Et	H	H
1-137	Pr	Me	H	H	Phth	H	H
1-138	Et	H	H	H	H	H	H
1-139	Et	H	H	H	$PivOCH_2$—	H	H
1-140	Et	H	H	H	Mod	H	H
1-141	Et	s	H	H	$EtcOCH_2$—	H	H
1-142	Et	H	H	H	1-(EtcO)Et	H	H
1-143	Et	H	H	H	Phth	H	H

TABLE 2

Cpd. No.	R^1	R^2	R^3	R^4	R^{5a}	R^6	R^7
2-1	Pr	Me	Me	H	H	H	2-Tz
2-2	Bu	Me	Me	H	H	H	2-Tz
2-3	Pn	Me	Me	H	H	H	2-Tz
2-4	—CH=CH—Et	Me	Me	H	H	H	2-Tz
2-5	Pr	Me	Me	Me	H	H	2-Tz
2-6	Bu	Me	Me	Me	H	H	2-Tz
2-7	Pr	Me	Me	H	Et	H	2-Tz
2-8	Bu	Me	Me	H	Et	H	2-Tz
2-9	Pr	Me	Me	H	Me	H	2-Tz
2-10	Bu	Me	Me	H	Me	H	2-Tz
2-11	Pr	Me	Me	Me	Me	H	2-Tz
2-12	Bu	Me	Me	Me	Me	H	2-Tz
2-13	Pr	Me	Me	Me	Et	H	2-Tz
2-14	Bu	Me	Me	Me	Et	H	2-Tz
2-15	Pr	Me	Me	H	$PivOCH_2$—	H	2-Tz
2-16	Bu	Me	Me	H	$PivOCH_2$—	H	2-Tz
2-17	Pr	Me	Me	H	Mod	H	2-Tz
2-18	Bu	Me	Me	H	Mod	H	2-Tz
2-19	Pr	Me	Me	H	$EtcOCH_2$—	H	2-Tz
2-20	Bu	Me	Me	H	$EtcOCH_2$—	H	2-Tz
2-21	Pr	Me	Me	H	$iPrcOCH_2$—	H	2-Tz
2-22	Bu	Me	Me	H	$iPrcOCH_2$—	H	2-Tz
2-23	Pr	Me	Me	H	1-(EtcO)Et	H	2-Tz
2-24	Bu	Me	Me	H	1-(EtcO)Et	H	2-Tz
2-25	Pr	Me	Me	H	1-(iPrcO)Et	H	2-Tz
2-26	Bu	Me	Me	H	1-(iPrcO)Et	H	2-Tz
2-27	Pr	Me	Me	Me	$EtcOCH_2$—	H	2-Tz
2-28	Bu	Me	Me	Me	$EtcOCH_2$—	H	2-Tz
2-29	Pr	Me	Me	Me	$iPrcOCH_2$—	H	2-Tz
2-30	Bu	Me	Me	Me	$iPrcOCH_2$—	H	2-Tz
2-31	Pr	Me	Me	Me	$PivOCH_2$—	H	2-Tz
2-32	Bu	Me	Me	Me	$PivOCH_2$—	H	2-Tz
2-33	Pr	Me	Me	H	H	6-Cl	2-Tz
2-34	Bu	Me	Me	H	H	6-Cl	2-Tz
2-35	Pr	Me	Me	H	H	6-OMe	2-Tz
2-36	Bu	Me	Me	H	H	6-OMe	2-Tz
2-37	Pr	Me	Et	H	H	H	2-Tz
2-38	Bu	Me	Et	H	H	H	2-Tz
2-39	Pr	Et	Et	H	H	H	2-Tz
2-40	Bu	Et	Et	H	H	H	2-Tz
2-41	Pr	Me	Me	H	Bz	H	2-Tz
2-42	Pr	Me	Me	H	Bu	H	2-Tz
2-43	Bu	Me	Me	H	Bz	H	2-Tz
2-44	Bu	Me	Me	H	Bu	H	2-Tz
2-45	Pr	Et	Et	H	Et	H	2-Tz
2-46	Pr	Me	Me	H	H	H	3-Tz
2-47	Pr	Me	Me	H	H	H	4-Tz
2-48	Pr	Me	Me	H	(4-OAc)-(3-OMe)Bz	H	2-Tz
2-49	Pr	Me	Me	H	Fo	H	2-Tz
2-50	Pr	Me	Me	H	Ac	H	2-Tz
2-51	Pr	Me	Me	H	H	6-Cl	3-Tz
2-52	Bu	Me	Me	H	H	6-Cl	3-Tz
2-53	Pr	Me	Me	H	H	6-OMe	3-Tz
2-54	Bu	Me	Me	H	H	6-OMe	3-Tz
2-55	Pr	Me	Et	H	H	H	3-Tz

TABLE 2-continued

Cpd. No.	R^1	R^2	R^3	R^4	R^{5a}	R^6	R^7
2-56	Bu	Me	Et	H	H	H	3-Tz
2-57	Pr	Et	Et	H	H	H	3-Tz
2-58	Bu	Et	Et	H	H	H	3-Tz
2-59	Pr	Me	Me	Me	Et	H	3-Tz
2-60	Pr	Me	Me	Me	H	H	3-Tz
2-61	Bu	Me	Me	Me	Et	H	3-Tz
2-62	Bu	Me	Me	Me	H	H	3-Tz
2-63	Pr	Et	Et	H	Et	H	3-Tz
2-64	Pr	Me	Et	Me	H	H	2-Tz
2-65	Pr	Me	Me	H	Phth	H	2-Tz
2-66	Pr	Me	Me	Me	Mod	H	2-Tz
2-67	Bu	Me	Me	Me	Mod	H	2-Tz
2-68	Et	Me	Me	H	H	H	2-Tz
2-69	Et	Me	Me	H	$PivOCH_2$—	H	2-Tz
2-70	Et	Me	Me	H	$EtcOCH_2$—	H	2-Tz
2-71	Et	Me	Me	H	$iPrcOCH_2$—	H	2-Tz
2-72	Et	Me	Me	H	Et	H	2-Tz
2-73	Et	Me	Me	H	Mod	H	2-Tz
2-74	Et	Me	Me	H	Phth	H	2-Tz
2-75	Et	Me	Me	Me	H	H	2-Tz
2-76	Et	Me	Me	Me	$PivOCH_2$—	H	2-Tz
2-77	Et	Me	Me	Me	Mod	H	2-Tz

TABLE 3

Cpd. No.	R^1	R^2	R^3	R^4	R^{5a}
3-1	Pr	Me	Me	H	$PivOCH_2$—
3-2	Pr	Me	Me	H	$AcOCH_2$—
3-3	Pr	Me	Me	H	1-(PivO)Et
3-4	Pr	Me	Me	H	1-(AcO)Et
3-5	Pr	Me	Me	H	cPnCO.OCH_2—
3-6	Pr	Me	Me	H	cHxCO.OCH_2—
3-7	Pr	Me	Me	H	$MecOCH_2$—
3-8	Pr	Me	Me	H	1-(MecO)Et
3-9	Pr	Me	Me	H	$EtcOCH_2$—
3-10	Pr	Me	Me	H	1-(EtcO)Et
3-11	Pr	Me	Me	H	1-(EtcO)-2-MePr
3-12	Pr	Me	Me	H	1-(EtcO)Pr
3-13	Pr	Me	Me	H	$iPrcOCH_2$—
3-14	Pr	Me	Me	H	1-(iPrcO)Et
3-15	Pr	Me	Me	H	1-(iPrcO)-2-MePr
3-16	Pr	Me	Me	H	1-(iPrcO)Pr
3-17	Pr	Me	Me	H	cPnO.CO.OCH_2—
3-18	pr	Me	Me	H	cHxO.CO.OCH_2—
3-19	Pr	Me	Me	H	$BucOCH_2$—
3-20	Pr	Me	Me	H	1-(BucO)Et
3-21	Pr	Me	Me	H	$iBucOCH_2$—
3-22	Pr	Me	Me	H	1-(iBucO)Et
3-23	Pr	Me	Me	H	1-(cPnO.CO.O)Et
3-24	Pr	Me	Me	H	1-(cHxO.CO.O)Et
3-25	Pr	Me	Me	H	Mod
3-26	Pr	Me	Me	H	Phth
3-27	Bu	Et	Et	H	$PivOCH_2$—
3-28	Bu	Me	Me	H	$AcOCH_2$—
3-29	Bu	Me	Me	H	1-(PivO)Et
3-30	Bu	Me	Me	H	1-(AcO)Et
3-31	Bu	Me	Me	H	cPnCO.OCH—
3-32	Bu	Me	Me	H	cHxCO.OCH_2—
3-33	Bu	Me	Me	H	$MecOCH_2$—
3-34	Bu	Me	Me	H	1-(MecO)Et
3-35	Bu	Me	Me	H	$EtcOCH_2$—
3-36	Bu	Me	Me	H	1-(EtcO)Et
3-37	Bu	Me	Me	H	1-(EtcO)-2-MePr
3-38	Bu	Me	Me	H	1-(EtcO)Pr
3-39	Bu	Me	Me	H	$iPrcOCH_2$—
3-40	Bu	Me	Me	H	1-(iPrcO)Et
3-41	Bu	Me	Me	H	1-(iPrcO)-2-MePr
3-42	Bu	Me	Me	H	1-(iPrcO)Pr
3-43	Bu	Me	Me	H	cPnO.CO.OCH_2—
3-44	Bu	Me	Me	H	cHxO.CO.OCH_2—
3-45	Bu	Me	Me	H	$BucOCH_2$—

TABLE 3-continued

Cpd. No.	R^1	R^2	R^3	R^4	R^{5a}
3-46	Bu	Me	Me	H	1-(BucO)Et
3-47	Bu	Me	Me	H	$iBucOCH_2$—
3-48	Bu	Me	Me	H	1-(iBucO)Et
3-49	Bu	Me	Me	H	1-(cPnO.CO.O)Et
3-50	Bu	Me	Me	H	1-(cHxO.CO.O)Et
3-51	Bu	Et	Et	H	Mod
3-52	Bu	Me	Me	H	Phth
3-53	Pr	Me	Me	Me	$PivOCH_2$—
3-54	Pr	Me	Me	Me	$AcOCH_2$—
3-55	Pr	Me	Me	Me	1-(PivO)Et
3-56	Pr	Me	Me	Me	1-(AcO)Et
3-57	Pr	Me	Me	Me	cPnCO.OCH_2—
3-58	Pr	Me	Me	Me	cHxCO.OCH_2—
3-59	Pr	Me	Me	Me	$MecOCH_2$—
3-60	Pr	Me	Me	Me	1-(MecO)Et
3-61	Pr	Me	Me	Me	$EtcOCH_2$—
3-62	Pr	Me	Me	Me	1-(EtcO)Et
3-63	Pr	Me	Me	Me	1-(EtcO)-2-MePr
3-64	Pr	Me	Me	Me	1-(EtcO)Pr
3-65	Pr	Me	Me	Me	$iPrcOCH_2$—
3-66	Pr	Me	Me	Me	1-(iPrcO)Et
3-67	Pr	Me	Me	Me	1-(iPrcO)-2-MePr
3-68	Pr	Me	Me	Me	1-(iPrcO)Pr
3-69	Pr	Me	Me	Me	cPnO.CO.OCH_2—
3-70	Pr	Me	Me	Me	cHxO.CO.OCH_2—
3-71	Pr	Me	Me	Me	$BucOCH_2$—
3-72	Pr	Me	Me	Me	1-(BucO)Et
3-73	Pr	Me	Me	Me	$iBucOCH_2$—
3-74	Pr	Me	Me	Me	1-(iBucO)Et
3-75	Pr	Me	Me	Me	1-(cPnO.CO.O)Et
3-76	Pr	Me	Me	Me	1-(cHxO.CO.O)Et
3-77	Pr	Me	Me	Me	Mod
3-78	Pr	Me	Me	Me	Phth
3-79	Bu	Me	Me	Me	$PivOCH_2$—
3-80	Bu	Me	Me	Me	$AcOCH_2$—
3-81	Bu	Me	Me	Me	1-(PivO)Et
3-82	Bu	Me	Me	Me	1-(AcO)Et
3-83	Bu	Me	Me	Me	cPnCO.OCH_2—
3-84	Bu	Me	Me	Me	cHxCO.OCH_2—
3-85	Bu	Me	Me	Me	$MecOCH_2$—
3-86	Bu	Me	Me	Me	1-(MecO)Et
3-87	Bu	Me	Me	Me	$EtcOCH_2$—
3-88	Bu	Me	Me	Me	1-(EtCO)Et
3-89	Bu	Me	Me	Me	1-(EtcO)-2-MePr
3-90	Bu	Me	Me	Me	1-(EtcO)Pr

TABLE 3-continued

Cpd. No.	R^1	R^2	R^3	R^4	R^{5a}
3-91	Bu	Me	Me	Me	$iPrcOCH_2$—
3-92	Bu	Me	Me	Me	1-(iPrcO)Et
3-93	Bu	Me	Me	Me	1-(iPrcO)-2-MePr
3-94	Bu	Me	Me	Me	1-(iPrcO)Pr
3-95	Bu	Me	Me	Me	cPnO.CO.OCH_2—
3-96	Bu	Me	Me	Me	cHxO.CO.OCH_2—
3-97	Bu	Me	He	Me	$BucOCH_2$—
3-98	Bu	Me	Me	Me	1-(BucO)Et
3-99	Bu	Me	Me	Me	iBucOCH—
3-100	Bu	Me	Me	Me	1-(iBucO)Et
3-101	Bu	Me	Me	Me	1-(cPnO.CO.O)Et
3-102	Bu	Me	Me	Me	1-(cHxO.CO.O)Et
3-103	Bu	Me	Me	Me	Mod
3-104	Bu	Me	Me	Me	Phth
3-105	Et	Me	Me	H	$PivOCH_2$—
3-106	Et	Me	Me	H	$AcOCH_2$—
3-107	Et	Me	Me	H	$EtcOCH_2$—
3-108	Et	Me	Me	H	1-(EtcO)Et
3-109	Et	Me	Me	H	$iPrcOCH_2$—
3-110	Et	Me	Me	H	1-(iPrcO)Et
3-111	Et	Me	Me	H	Mod
3-112	Et	Me	Me	H	Phth
3-113	Pn	Me	Me	H	$PivOCH_2$—
3-114	Pn	Me	Me	H	$AcOCH_2$—
3-115	Pn	Me	Me	H	$EtcOCH_2$—
3-116	Pn	Me	Me	H	1-(EtCO)Et
3-117	Pn	Me	Me	H	$iPrcOCH_2$—
3-118	Pn	Me	Me	H	1-(iPrcO)Et
3-119	Pn	Me	Me	H	Mod
3-120	Pn	Me	Me	H	Phth
3-121	Pr	Me	Et	H	$PivOCH_2$—
3-122	Pr	Me	Et	H	$AcOCH_2$—
3-123	Pr	Me	Et	H	$EtcOCH_2$—
3-124	Pr	Me	Et	H	1-(EtcO)Et
3-125	Pr	Me	Et	H	$iPrcOCH_2$—
3-126	Pr	Me	Et	H	1-(iPrcO)Et
3-127	Pr	Me	Et	H	Mod
3-128	Pr	Me	Et	H	Phth
3-129	Pr	Et	Et	H	$PivOCH_2$—
3-130	Pr	Et	Et	H	$AcOCH_2$—
3-131	Pr	Et	Et	H	$EtcOCH_2$—
3-132	Pr	Et	Et	H	1-(EtcO)Et
3-133	Pr	Et	Et	H	$iPrcOCH_2$—
3-134	Pr	Et	Et	H	1-(iPrcO)Et
3-135	Pr	Et	Et	H	Mod
3-136	Pr	Et	Et	H	Phth

TABLE 4

Cpd. No.	R^1	R^2	R^4	R^{5a}
4-1	Pr	H	H	H
4-2	Pr	H	H	Me
4-3	Pr	H	H	Et
4-4	Pr	H	H	$PivOH_2$—
4-5	Pr	H	H	Mod
4-6	Pr	H	H	$EtcOCH_2$—
4-7	Pr	H	H	$iPrcOCH_2$—
4-8	Pr	H	H	1-(EtcO)Et
4-9	Pr	H	H	1-(iPrcO)Et
4-10	Pr	H	H	Phth
4-11	Pr	H	Me	H
4-12	Pr	H	Me	Me
4-13	Pr	H	Me	Et
4-14	Pr	H	Me	$PivOCH_2$—
4-15	Pr	H	Me	Mod
4-16	Pr	H	Me	$EtcOCH_2$—
4-17	Pr	H	Me	$iPrcOCH_2$—
4-18	Pr	H	Me	1-(EtcO)Et
4-19	Pr	H	Me	1-(iPrcO)Et
4-20	Pr	H	Me	Phth
4-21	Pr	H	Fo	H
4-22	Pr	H	Fo	$PivOCH_2$—

TABLE 4-continued

Cpd. No.	R^1	R^2	R^4	R^{5a}
4-23	Pr	H	Fo	Mod
4-24	Pr	H	Fo	Phth
4-25	Pr	H	Ac	H
4-26	Pr	H	Ac	$PivOCH_2$—
4-27	Pr	H	Ac	Mod
4-28	Pr	H	Ac	Phth
4-29	Pr	Me	H	H
4-30	Pr	Me	H	Et
4-31	Pr	Me	H	$PivOCH_2$—
4-32	Pr	Me	H	Mod
4-33	Pr	Me	H	$EtcOCH_2$—
4-34	Pr	Me	H	$iPrcOCH_2$—
4-35	Pr	Me	H	Phth
4-36	Pr	Me	Me	H
4-37	Pr	Me	Me	Et
4-38	Pr	Me	Me	$PivOCH_2$—
4-39	Pr	Me	Me	Mod
4-40	Pr	Me	Me	Phth
4-41	Pr	Et	H	H
4-42	Pr	Et	H	Et
4-43	Pr	Et	H	$PivOCH_2$—
4-44	Pr	Et	H	Mod
4-45	Pr	Et	H	Phth
4-46	Bu	H	H	H
4-47	Bu	H	H	Me
4-48	Bu	H	H	Et
4-49	Bu	H	H	$PivOCH_2$—
4-50	Bu	H	H	Mod
4-51	Bu	H	H	$EtcOCH_2$—
4-52	Bu	H	H	$iPrcOCH_2$—
4-53	Bu	H	H	1-(EtcO)Et
4-54	Bu	H	H	1-(iPrcO)Et
4-55	Bu	H	H	Phth
4-56	Bu	H	Me	H
4-57	Bu	H	Me	Me
4-58	Bu	H	Me	Et
4-59	Bu	H	Me	$PivOCH_2$—
4-60	Bu	H	Me	Mod
4-61	Bu	H	Me	$EtcOCH_2$—
4-62	Bu	H	Me	$iPrcOCH_2$—
4-63	Bu	H	Me	1-(EtcO)Et
4-64	Bu	H	Me	1-(iPrco)Et
4-65	Bu	H	Me	Phth
4-66	Bu	H	Fo	H
4-67	Bu	H	Fo	$PivOCH_2$—
4-68	Bu	H	Fo	Mod
4-69	Bu	H	Fo	Phth
4-70	Bu	H	Ac	H
4-71	Bu	H	Ac	$PivOCH_2$—
4-72	Bu	H	Ac	Mod
4-73	Bu	H	Ac	Phth
4-74	Bu	Me	H	H
4-75	Bu	Me	H	Et
4-76	Bu	Me	H	$PivOCH_2$—
4-77	Bu	Me	H	Mod
4-78	Bu	Me	H	$EtcOCH_2$—
4-79	Bu	Me	H	$iPrcOCH_2$—
4-80	Bu	Me	H	Phth
4-81	Bu	Me	Me	H
4-82	Bu	Me	Me	Me
4-83	Bu	Me	Me	$PivOCH_2$—
4-84	Bu	Me	Me	Mod
4-85	Bu	Me	Me	Phth
4-86	Bu	Et	H	H
4-87	Bu	Et	H	Me
4-88	Bu	Et	H	$PivOCH_2$—
4-89	Bu	Et	H	Mod
4-90	Bu	Et	H	Phth
4-91	Et	H	H	H
4-92	Et	H	Et	H
4-93	Et	H	Et	$PivOCH_2$—
4-94	Et	H	Et	Mod
4-95	Et	H	Et	Phth
4-96	Pn	H	H	H
4-97	Pn	H	H	Et
4-98	Pn	H	H	$PivOCH_2$—

TABLE 4-continued

Cpd. No.	R^1	R^2	R^4	R^{5a}
4-99	Pn	H	H	Mod
4-100	Pn	H	H	Phth
4-101	Pr	iPr	H	H
4-102	Pr	iPr	H	$PivOCH_2$—
4-103	Pr	iPr	H	Mod
4-104	Pr	tBu	H	H
4-105	Pr	tBu	H	$PivOCH_2$—
4-106	Pr	tBu	H	Mod
4-107	Et	Me	H	H
4-108	Et	Me	H	Et
4-109	Et	Me	H	$PivOCH_2$—
4-110	Et	Me	H	Mod
4-111	Et	Me	H	Phth
4-112	Et	H	H	$PivOCH_2$—
4-113	Et	H	H	Mod
4-114	Et	Me	H	$PivOCH_2$—
4-115	Et	Me	H	Mod

TABLE 5

Cpd. No.	R^1	R^2	R^3	R^6	R^7	R^8	R^9
5-1	Pr	H	H	H	COOH	H	H
5-2	Pr	Me	H	H	COOH	H	H
5-3	Pr	Et	H	H	COOH	H	H
5-4	Pr	Pr	H	H	COOH	H	H
5-5	Pr	iPr	H	H	COOH	H	H
5-6	Pr	tBu	H	H	COOH	H	H
5-7	Pr	Me	Me	H	COOH	H	H
5-8	Pr	Me	Et	H	COOH	H	H
5-9	Pr	H	H	Me	COOH	H	H
5-10	Pr	H	H	Et	COOH	H	H
5-11	Pr	Me	H	Me	COOH	H	H
5-12	Pr	Et	H	Me	COOH	H	H
5-13	Pr	iPr	H	Me	COOH	H	H
5-14	Pr	tBu	H	Me	COOH	H	H
5-15	Pr	H	H	Fo	COOH	H	H
5-16	Pr	Me	H	Fo	COOH	H	H
5-17	Pr	Et	H	Fo	COOH	H	H
5-18	Pr	iPr	H	Fo	COOH	H	H
5-19	Pr	tBu	H	Fo	COOH	H	H
5-20	Pr	H	H	Ac	COOH	H	H
5-21	Pr	Me	H	Ac	COOH	H	H
5-22	Pr	Et	H	Ac	COOH	H	H
5-23	Pr	iPr	H	Ac	COOH	H	H
5-24	Pr	tBu	H	Ac	COOH	H	H
5-25	Pr	H	H	H	COOH	H	Me
5-26	Pr	H	H	H	COOH	H	Et
5-27	Pr	H	H	H	COOH	H	Pr
5-28	Pr	H	H	H	COOH	H	iPr
5-29	Pr	H	H	H	COOH	H	iBu
5-30	Pr	H	H	H	COOH	H	iPn
5-31	Pr	H	H	H	COOH	Me	Me
5-32	Pr	H	H	H	Tz	H	H
5-33	Pr	Me	H	H	Tz	H	H
5-34	Pr	Et	H	H	Tz	H	H
5-35	Pr	Pr	H	H	Tz	H	H
5-36	Pr	iPr	H	H	Tz	H	H
5-37	Pr	tBu	H	H	Tz	H	H
5-38	Pr	Me	Me	H	Tz	H	H
5-39	Pr	Me	Et	H	Tz	H	H
5-40	Pr	H	H	Me	Tz	H	H
5-41	Pr	H	H	Et	Tz	H	H
5-42	Pr	Me	H	Me	Tz	H	H
5-43	Pr	Et	H	Me	Tz	H	H
5-44	Pr	iPr	H	Me	Tz	H	H
5-45	Pr	tBu	H	Me	Tz	H	H
5-46	Pr	H	H	Fo	Tz	H	H
5-47	Pr	Me	H	Fo	Tz	H	H
5-48	Pr	Et	H	Fo	Tz	H	H
5-49	Pr	iPr	H	Fo	Tz	H	H
5-50	Pr	tBu	H	Fo	Tz	H	H
5-51	Pr	H	H	Ac	Tz	H	H
5-52	Pr	Me	H	Ac	Tz	H	H
5-53	Pr	Et	H	Ac	Tz	H	H
5-54	Pr	iPr	H	Ac	Tz	H	H
5-55	Pr	tBu	H	Ac	Tz	H	H
5-56	Pr	H	H	H	Tz	H	Me
5-57	Pr	H	H	H	Tz	H	Et
5-58	Pr	H	H	H	Tz	H	Pr
5-59	Pr	H	H	H	Tz	H	iPr

TABLE 5-continued

Cpd. No.	R^1	R^2	R^3	R^4	R^7	R^8	R^9
5-60	Pr	H	H	H	Tz	H	tBu
5-61	Pr	H	H	H	Tz	H	iPn
5-62	Pr	H	H	H	Tz	Me	Me
5-63	Bu	H	H	H	COOH	H	H
5-64	Bu	Me	H	H	COOH	H	H
5-65	Bu	Et	H	H	COOH	H	H
5-66	Bu	Pr	H	H	COOH	H	H
5-67	Bu	iPr	H	H	COOH	H	H
5-68	Bu	tBu	H	H	COOH	H	H
5-69	Bu	Me	Me	H	COOH	H	H
5-70	Bu	Me	Et	H	COOH	H	H
5-71	Bu	H	H	Me	COOH	H	H
5-72	Bu	H	H	Et	COOH	H	H
5-73	Bu	Me	H	Me	COOH	H	H
5-74	Bu	Et	H	Me	COOH	H	H
5-75	Bu	iPr	H	Me	COOH	H	H
5-76	Bu	tBu	H	Me	COOH	H	H
5-77	Bu	H	H	Fo	COOH	H	H
5-78	Bu	Me	H	Fo	COOH	H	H
5-79	Bu	Et	H	Fo	COOH	H	H
5-80	Bu	iPr	H	Fo	COOH	H	H
5-81	Bu	tBu	H	Fo	COOH	H	H
5-82	Bu	H	H	Ac	COOH	H	H
5-83	Bu	Me	H	Ac	COOH	H	H
5-84	Bu	Et	H	Ac	COOH	H	H
5-85	Bu	iPr	H	Ac	COOH	H	H
5-86	Bu	tBu	H	Ac	COOH	H	H
5-87	Bu	H	H	H	COOH	H	Me
5-88	Bu	H	H	H	COOH	H	Et
5-89	Bu	H	H	H	COOH	H	Pr
5-90	Bu	H	H	H	COOH	H	iPr
5-91	Bu	H	H	H	COOH	H	tBu
5-92	Bu	H	H	H	COOH	H	iPn
5-93	Bu	H	H	H	COOH	Me	Me
5-94	Bu	H	H	H	Tz	H	H
5-95	Bu	Me	H	H	Tz	H	H
5-96	Bu	Et	H	H	Tz	H	H
5-97	Bu	Pr	H	H	Tz	H	H
5-98	Bu	iPr	H	H	Tz	H	H
5-99	Bu	tBu	H	H	Tz	H	H
5-100	Bu	Me	Me	H	Tz	H	H
5-101	Bu	Me	Et	H	Tz	H	H
5-102	Bu	H	H	Me	Tz	H	H
5-103	Bu	H	H	Et	Tz	H	H
5-104	Bu	Me	H	Me	Tz	H	H
5-105	Bu	Et	H	Me	Tz	H	H
5-106	Bu	iPr	H	Me	Tz	H	H
5-107	Bu	tBu	H	Me	Tz	H	H
5-108	Bu	H	H	Fo	Tz	H	H
5-109	Bu	Me	H	Fo	Tz	H	H
5-110	Bu	Et	H	Fo	Tz	H	H
5-111	Bu	iPr	H	Fo	Tz	H	H
5-112	Bu	tBu	H	Fo	Tz	H	H
5-113	Bu	H	H	Ac	Tz	H	H
5-114	Bu	Me	H	Ac	Tz	H	H
5-115	Bu	Et	H	Ac	Tz	H	H
5-116	Bu	iPr	H	Ac	Tz	H	H
5-117	Bu	tBu	H	Ac	Tz	H	H
5-118	Bu	H	H	H	Tz	H	Me
5-119	Bu	H	H	H	Tz	H	Et
5-120	Bu	H	H	H	Tz	H	Pr
5-121	Bu	H	H	H	Tz	H	iPr
5-122	Bu	H	H	H	Tz	H	iBu
5-123	Bu	H	H	H	Tz	H	iPn
5-124	Bu	H	H	H	Tz	Me	Me
5-125	Bu	H	H	H	COOH	H	CH_2COOH
5-126	Bu	H	H	H	COOH	H	CH_2COOEt
5-127	Bu	H	H	H	COOH	H	1-(HOOC)Et
5-128	Bu	H	H	H	COOH	H	1-(Etc)Et
5-129	Bu	H	H	H	COOH	H	2-(HOOC)Et
5-130	Bu	H	H	H	COOH	H	2-(Etc)Et
5-131	Bu	H	H	H	COOH	H	α-(HOOC)Bz
5-132	Bu	H	H	H	COOH	H	1-(HOOC)-2-(Ph)Et
5-133	Bu	H	H	H	COOH	H	1-(HOOC)-2-(Fu)Et
5-134	Bu	H	H	H	COOH	H	1-(HOOC)-2-(Th)Et
5-135	Bu	H	H	H	COOH	H	1-(HOOC)-2-(Im)Et

TABLE 5-continued

Cpd. No.	R^1	R^2	R^3	R^4	R^7	R^8	R^9
5-136	Bu	H	H	H	COOH	H	1-(HOOC)-2-(HO)Et
5-137	Bu	H	H	H	COOH	H	1-(HOOC)-2-(MeO)Et
5-138	Bu	Me	H	H	COOH	H	CH_2COOH
5-139	Bu	Me	H	H	COOH	H	CH_2COOEt
5-140	Bu	Me	H	H	COOH	H	1-(HOOC)Et
5-141	Bu	Me	H	H	COOH	H	1-(Etc)Et
5-142	Bu	Me	H	H	COOH	H	2-(HOOC)Et
5-143	Bu	Me	H	H	COOH	H	2-(Etc)Et
5-144	Bu	Me	H	H	COOH	H	α-(HOOC)-Bz
5-145	Bu	Me	H	H	COOH	H	1-(HOOC)-2-(Ph)Et
5-146	Bu	Me	H	H	COOH	H	1-(HOOC)-2-(Fu)Et
5-147	Bu	Me	H	H	COOH	H	1-(HOOC)-2-(Th)Et
5-148	Bu	Me	H	H	COOH	H	1-(HOOC)-2-(Im)Et
5-149	Bu	Me	H	H	COOH	H	1-(HOOC)-2-(HO)Et
5-150	Bu	Me	H	H	COOH	H	1-(HOOC)-2-(MeO)Et
5-151	Bu	iPr	H	H	COOH	H	CH_2COOH
5-152	Bu	iPr	H	H	COOH	H	CH_2COOEt
5-153	Bu	iPr	H	H	COOH	H	1-(HOOC)Et
5-154	Bu	iPr	H	H	COOH	H	1-(Etc)Et
5-155	Bu	iPr	H	H	COOH	H	2-(HOOC)Et
5-156	Bu	iPr	H	H	COOH	H	2-(Etc)Et
5-157	Bu	iPr	H	H	COOH	H	α-(HOOC)-Bz
5-158	Bu	iPr	H	H	COOH	H	1-(HOOC)-2-(Ph)Et
5-159	Bu	iPr	H	H	COOH	H	1-(HOOC)-2-(Fu)Et
5-160	Bu	iPr	H	H	COOH	H	1-(HOOC)-2-(Th)Et
5-161	Bu	iPr	H	H	COOH	H	1-(HOOC)-2-(Im)Et
5-162	Bu	iPr	H	H	COOH	H	1-(HOOC)-2-(HO)Et
5-163	Bu	iPr	H	H	COOH	H	1-(HOOC)-2-(MeO)Et
5-164	Bu	tBu	H	H	COOH	H	CH_2COOH
5-165	Bu	tBu	H	H	COOH	H	CH_2COOEt
5-166	Bu	tBu	H	H	COOH	H	1-(HOOC)Et
5-167	Bu	tBu	H	H	COOH	H	1-(Etc)Et
5-168	Bu	tBu	H	H	COOH	H	2-(HOOC)Et
5-169	Bu	tBu	H	H	COOH	H	2-(Etc)Et
5-170	Bu	tBu	H	H	COOH	H	α-(HOOC)-Bz
5-171	Bu	tBu	H	H	COOH	H	1-(HOOC)-2-(Ph)
5-172	Bu	tBu	H	H	COOH	H	1-(HOOC)-2-(Fu
5-173	Bu	tBu	H	H	COOH	H	1-(HOOC)-2-(Th)Et
5-174	Bu	tBu	H	H	COOH	H	1-(HOOC)-2-(Im)Et
5-175	Bu	tBu	H	H	COOH	H	1-(HOOC)-2-(HO)Et
5-176	Bu	tBu	H	H	COOH	H	1-(HOOC)-2-(MeO)Et
5-177	Bu	H	H	H	Tz	H	CH_2COOH
5-178	Bu	H	H	H	Tz	H	CH_2COOEt
5-179	Bu	H	H	H	Tz	H	1-(HOOC)Et
5-180	Bu	H	H	H	Tz	H	1-(Etc)Et
5-181	Bu	H	H	H	Tz	H	2-(HOOC)Et
5-182	Bu	H	H	H	Tz	H	2-(Etc)Et
5-183	Bu	H	H	H	Tz	H	α-(HOOC)-Bz
5-184	Bu	H	H	H	Tz	H	1-(HOOC)-2-(Ph)Et
5-185	Bu	H	H	H	Tz	H	1-(HOOC)-2-(Fu)Et
5-186	Bu	H	H	H	Tz	H	1-(HOOC)-2-(Th)Et
5-187	Bu	H	H	H	Tz	H	1-(HOOC)-2-(Im)Et
5-188	Bu	H	H	H	Tz	H	1-(HOOC)-2-(HO)Et
5-189	Bu	H	H	H	Tz	H	1-(HOOC)-2-(MeO)Et
5-190	Bu	Me	H	H	Tz	H	CH_2COOH
5-191	Bu	Me	H	H	Tz	H	CH_2COOEt
5-192	Bu	Me	H	H	Tz	H	1-(HOOC)Et
5-193	Bu	Me	H	H	Tz	H	1-(Etc)Et
5-194	Bu	Me	H	H	Tz	H	2-(HOOC)Et
5-195	Bu	Me	H	H	Tz	H	2-(Etc)Et
5-196	Bu	Me	H	H	Tz	H	α-(HOOC)-Bz
5-197	Bu	Me	H	H	Tz	H	1-(HOOC)-2-(Ph)Et
5-198	Bu	Me	H	H	Tz	H	1 (HOOC)-2-(Fu)Et-
5-199	Bu	Me	H	H	Tz	H	1-(ROOC)-2-(Th)Et
5-200	Bu	Me	H	H	Tz	H	1-(HOOC)-2-(Im)Et
5-201	Bu	Me	H	H	Tz	H	1-(HOOC)-2-(HO)Et
5-202	Bu	Me	H	H	Tz	H	1-(HOOC)-2-(MeO)Et
5-203	Bu	iPr	H	H	Tz	H	CH_2COOH
5-204	Bu	iPr	H	H	Tz	H	CH_2COOEt
5-205	Bu	iPr	H	H	Tz	H	1-(HOOC)Et
5-206	Bu	iPr	H	H	Tz	H	1-(Etc)Et
5-207	Bu	iPr	H	H	Tz	H	2-(HOOC)Et
5-208	Bu	iPr	H	H	Tz	H	2-(Etc)Et
5-209	Bu	iPr	H	H	Tz	H	α-(HOOC)-Bz
5-210	Bu	iPr	H	H	Tz	H	1-(HOOC)-2-(Ph)Et
5-211	Bu	iPr	H	H	Tz	H	1-(HOOC)-2-(Fu)Et

TABLE 5-continued

Cpd. No.	R^1	R^2	R^3	R^4	R^7	R^8	R^9
5-212	Bu	iPr	H	H	Tz	H	1-(HOOC)-2-(Th)Et
5-213	Bu	iPr	H	H	Tz	H	1-(HOOC)-2-(Im)Et
5-214	Bu	iPr	H	H	Tz	H	1-(HOOC)-2-(HO)Et
5-215	Bu	iPr	H	H	Tz	H	1-(HOOC)-2-(MeO)Et
5-216	Bu	tBu	H	H	Tz	H	CH_2COOH
5-217	Bu	tBu	H	H	Tz	H	CH_2COOEt
5-218	Bu	tBu	H	H	Tz	H	1-(HOOC)Et
5-219	Bu	tBu	H	H	Tz	H	1-(Etc)Et
5-220	Bu	tBu	H	H	Tz	H	2-(HOOC)Et
5-221	Bu	tBu	H	H	Tz	H	2-(Etc)Et
5-222	Bu	tBu	H	H	Tz	H	α-(HOOC)-Bz
5-223	Bu	tBu	H	H	Tz	H	1-(HOOC)-2-(Ph)Et
5-224	Bu	tBu	H	H	Tz	H	1-(HOOC)-2-(Fu)Et
5-225	Bu	tBu	H	H	Tz	H	1-(HOOC)-2-(Th)Et
5-226	Bu	tBu	H	H	Tz	H	1-(HOOC)-2-(Im)Et
5-227	Bu	tBu	H	H	Tz	H	1-(HOOC)-2-(HO)Et
5-228	Bu	tBu	H	H	Tz	H	1-(HOOC)-2-(MeO)Et
5-229	Pr	H	H	H	COOH	H	CH_2COOH
5-230	Pr	H	H	H	COOH	H	CH_2COOEt
5-231	Pr	H	H	H	COOH	H	1-(HOOC)Et
5-232	Pr	H	H	H	COOH	H	1-(Etc)Et
5-233	Pr	H	H	H	COOH	H	2-(HOOC)Et
5-234	Pr	H	H	H	COOH	H	2-(Etc)Et
5-235	Pr	H	H	H	COOH	H	α-(HOOC)-Bz
5-236	Pr	H	H	H	COOH	H	1-(HOOC)-2-(Ph)Et
5-237	Pr	H	H	H	COOH	H	1-(HOOC)-2-(Fu)Et
5-238	Pr	H	H	H	COOH	H	1-(HOOC)-2-(Th)Et
5-239	Pr	H	H	H	COOH	H	1-(HOOC)-2-(Im)Et
5-240	Pr	H	H	H	COOH	H	1-(HOOC)-2-(HO)Et
5-241	Pr	H	H	H	COOH	H	1-(HOOC)-2-(MeO)Et
5-242	Pr	Me	H	H	COOH	H	CH_2COOH
5-243	Pr	Me	H	H	COOH	H	CH_2COOEt
5-244	Pr	Me	H	H	COOH	H	1-(HOOC)Et
5-245	Pr	Me	H	H	COOH	H	1-(Etc)Et
5-246	Pr	Me	H	H	COOH	H	2-(HOOC)Et
5-247	Pr	Me	H	H	COOH	H	2-(Etc)Et
5-248	Pr	Me	H	H	COOH	H	α-(HOOC)-Bz
5-249	Pr	Me	H	H	COOH	H	1-(HOOC)-2-(Ph)Et
5-250	Pr	Me	H	H	COOH	H	1-(HOOC)-2-(Fu)Et
5-251	Pr	Me	H	H	COOH	H	1-(HOOC)-2-(Th)Et
5-252	Pr	Me	H	H	COOH	H	1-(HOOC)-2-(Im)Et
5-253	Pr	Me	H	H	COOH	H	1-(HOOC)-2-(HO)Et
5-254	Pr	Me	H	H	COOH	H	1-(HOOC)-2-(MeO)Et
5-255	Pr	iPr	H	H	COOH	H	CH_2COOH
5-256	Pr	iPr	H	H	COOH	H	CH_2COOEt
5-257	Pr	iPr	H	H	COOH	H	1-(HOOC)Et
5-258	Pr	iPr	H	H	COOH	H	1-(Etc)Et
5-259	Pr	iPr	H	H	COOH	H	2-(HOOC)Et
5-260	Pr	iPr	H	H	COOH	H	2-(Etc)Et
5-261	Pr	iPr	H	H	COOH	H	$CH_2(Ph)COOH$
5-262	Pr	iPr	H	H	COOH	H	1-(HOOC)-2-(Ph)Et
5-263	Pr	iPr	H	H	COOH	H	1-(HOOC)-2-(FU)Et
5-264	Pr	iPr	H	H	COOH	H	1-(HOOC)-2-(Th)Et
5-265	Pr	iPr	H	H	COOH	H	1-(HOOC)-2-(Im)Et
5-266	Pr	iPr	H	H	COOH	H	1-(HOOC)-2-(HO)Et
5-267	Pr	iPr	H	H	COOH	H	1-(HOOC)-2-(MeO)Et
5-268	Pr	tBu	H	H	COOH	H	CH_2COOH
5-269	Pr	tBu	H	H	COOH	H	CH_2COOEt
5-270	Pr	tBu	H	H	COOH	H	1-(HOOC)Et
5-271	Pr	tBu	H	H	COOH	H	1-(Etc)Et
5-272	Pr	tBu	H	H	COOH	H	2-(HOOC)Et
5-273	Pr	tBu	H	H	COOH	H	2-(Etc)Et
5-274	Pr	tBu	H	H	COOH	H	α-(HOOC)-Bz
5-275	Pr	tBu	H	H	COOH	H	1-(HOOC)-2-(Ph)Et
5-276	Pr	tBu	H	H	COOH	H	1-(HOOC)-2-(Fu)Et
5-277	Pr	tBu	H	H	COOH	H	1-(HOOC)-2-(Th)Et
5-278	Pr	tBu	H	H	COOH	H	1-(HOOC)-2-(Im)Et
5-279	Pr	tBu	H	H	COOH	H	1-(HOOC)-2-(HO)Et
5-280	Pr	tBu	H	H	COOH	H	1-(HOOC)-2-(MeO)Et
5-281	Pr	H	H	H	Tz	H	CH_2COOH
5-282	Pr	H	H	H	Tz	H	CH_2COOEt
5-283	Pr	H	H	H	Tz	H	1-(HOOC)Et
5-284	Pr	H	H	H	Tz	H	1-(Etc)Et
5-285	Pr	H	H	H	Tz	H	2-(HOOC)Et
5-286	Pr	H	H	H	Tz	H	2-(Etc)Et
5-287	Pr	H	H	H	Tz	H	α-(HOOC)-Bz

TABLE 5-continued

Cpd. No.	R^1	R^2	R^3	R^4	R^7	R^8	R^9
5-288	Pr	H	H	H	Tz	H	1-(HOOC)-2-(Ph)Et
5-289	Pr	H	H	H	Tz	H	1-(HOOC)-2-(Fu)Et
5-290	Pr	H	H	H	Tz	H	1-(HOOC)-2-(Th)Et
5-291	Pr	H	H	H	Tz	H	1-(HOOC)-2-(Im)Et
5-292	Pr	H	H	H	Tz	H	1-(HOOC)-2-(HO)Et
5-293	Pr	H	H	H	Tz	H	1-(HOOC)-2-(MeO)Et
5-294	Pr	Me	H	H	Tz	H	CH_2COOH
5-295	Pr	Me	H	H	Tz	H	CH_2COOEt
5-296	Pr	Me	H	H	Tz	H	1-(HOOC)Et
5-297	Pr	Me	H	H	Tz	H	1-(Etc)Et
5-298	Pr	Me	H	H	Tz	H	2-(HOOC)Et
5-299	Pr	Me	H	H	Tz	H	2-(Etc)Et
5-300	Pr	Me	H	H	Tz	H	α-(HOOC)-Bz
5-301	Pr	Me	H	H	Tz	H	1-(HOOC)-2-(Ph)Et
5-302	Pr	Me	H	H	Tz	H	1-(HOOC)-2-(Fu)Et
5-303	Pr	Me	H	H	Tz	H	1-(HOOC)-2-(Th)Et
5-304	Pr	Me	H	H	Tz	H	1-(HOOC)-2-(Im)Et
5-305	Pr	Me	H	H	Tz	H	1-(HOOC)-2-(HO)Et
5-306	Pr	Me	H	H	Tz	H	1-(HOOC)-2-(MeO)Et
5-307	Pr	iPr	H	H	Tz	H	CH_2COOH
5-308	Pr	iPr	H	H	Tz	H	CH_2COOEt
5-309	Pr	iPr	H	H	Tz	H	1-(HOOC)Et
5-310	Pr	iPr	H	H	Tz	H	1-(Etc)Et
5-311	Pr	iPr	H	H	Tz	H	2-(HOOC)Et
5-312	Pr	iPr	H	H	Tz	H	2-(Etc)Et
5-313	Pr	iPr	H	H	Tz	H	α-(HOOC)-Bz
5-314	Pr	iPr	H	H	Tz	H	1-(HOOC)-2-(Ph)Et
5-315	Pr	iPr	H	H	Tz	H	1-(HOOC)-2-(Fu)Et
5-316	Pr	iPr	H	H	Tz	H	1-(HOOC)-2-(Th)Et
5-317	Pr	iPr	H	H	Tz	H	1-(HOOC)-2-(Im)Et
5-318	Pr	iPr	H	H	Tz	H	1-(HOOC)-2-(HO)Et
5-319	Pr	iPr	H	H	Tz	H	1-(HOOC)-2-(MeO)Et
5-320	Pr	tBu	H	H	Tz	H	CH_2COOH
5-321	Pr	tBu	H	H	Tz	H	CH_2COOEt
5-322	Pr	tBu	H	H	Tz	H	1-(HOOC)Et
5-323	Pr	tBu	H	H	Tz	H	1-(Etc)Et
5-324	Pr	tBu	H	H	Tz	H	2-(HOOC)Et
5-325	Pr	tBu	H	H	Tz	H	2-(Etc)Et
5-326	Pr	tBu	H	H	Tz	H	α-(HOOC)-Bz
5-327	Pr	tBu	H	H	Tz	H	1-(HOOC)-2-(Ph)Et
5-328	Pr	tBu	H	H	Tz	H	1-(HOOC)-2-(Fu)Et
5-329	Pr	tBu	H	H	Tz	H	1-(HOOC)-2-(Th)Et
5-330	Pr	tBu	H	H	Tz	H	1-(HOOC)-2-(Im)Et
5-331	Pr	tBu	H	H	Tz	H	1-(HOOC)-2-(HO)Et
5-332	Pr	tBu	H	H	Tz	H	1-(HOOC)-2-(MeO)Et
5-333	Bu	iPr	iPr	H	COOH	H	H
5-334	Bu	H	H	H	COOH		$-(CH_2)_3CH(COOH)-$
5-335	Bu	H	H	H	COOH		$-(CH_2)_3CH(COOMe)-$
5-336	Pr	H	H	H	$-COOCH_2-$ —OPiv	H	H
5-337	Pr	Me	H	H	$-COOCH_2OPiv$	H	H
5-338	Pr	Me	Me	H	$-COOCH_2OPiv$	H	H
5-339	Pr	H	H	H	—COOMod	H	H
5-340	Pr	Me	H	H	—COOMod	H	H
5-341	Pr	Me	Me	H	—COOMod	H	H
5-342	Bu	H	H	H	$-COOCH_2OPiv$	H	H
5-343	Bu	Me	H	H	$-CODCH_2OPiv$	H	H
5-344	Bu	Me	Me	H	$-COOCH_2OPiv$	H	H
5-345	Bu	H	H	H	—COOMod	H	H
5-346	Bu	Me	H	H	—COOMod	H	H
5-347	Bu	Me	Me	H	—COOMod	H	H
5-348	Et	iPr	H	H	Tz	H	H
5-349	Et	iPr	H	H	COOH	H	H
5-350	Et	tBu	H	H	Tz	H	H
5-351	Et	tBu	H	H	COOH	H	H

TABLE 6

Cpd. No.	R^1	R^2	R^3	R^4	R^{5a}	R^6	R^7
6-1	Pr	Me	Me	H	H	H	2-Tz
6-2	Pr	Me	Me	H	H	6-Cl	2-Tz

TABLE 6-continued

Cpd. No.	R^1	R^2	R^3	R^4	R^{5a}	R^6	R^7
6-3	Bu	me	Me	H	H	6-Cl	2-Tz
6-4	Pr	Me	Me	H	H	6-OMe	2-Tz

TABLE 6-continued

Cpd. No.	R^1	R^2	R^3	R^4	R^{5a}	R^6	R^7
6-5	Bu	Me	Me	H	H	6-OMe	2-Tz
6-6	Pr	Me	Et	H	H	H	2-Tz
6-7	Bu	Me	Et	H	H	H	2-Tz
6-8	Pr	Et	Et	H	H	H	2-Tz
6-9	Bu	Et	Et	H	H	H	2-Tz
6-10	Pr	Me	Me	Me	Et	H	2-Tz
6-11	Pr	Me	Me	Me	H	H	2-Tz
6-12	Bu	Me	Me	Me	Et	H	2-Tz
6-13	Bu	Me	Me	Me	H	H	2-Tz
6-14	Pr	Et	Et	H	Et	H	2-Tz
6-15	Et	Me	Me	H	H	H	2-Tz
6-16	Et	Me	Me	H	Et	H	2-Tz
6-17	Et	Me	Me	H	$iPrcOCH_2$—	H	2-Tz
6-18	Et	Me	Me	H	$PivOCH_2$—	H	2-Tz
6-19	Et	Me	Me	H	Mod	H	2-Tz
6-20	Et	Me	Me	H	Phth	H	2-Tz

Of the compounds listed above, the following are preferred, that is to say Compounds No. 1-1, 1-2, 1-3, 1-9, 1-11, 1-12, 1-15, 1-22, 1-23, 1-24, 1-25, 1-27, 1-28, 1-31, 1-35, 1-36, 1-37, 1-39, 1-41, 1-49, 1-54, 1-56, 1-58, 1-59, 1-60, 1-61, 1-62, 1-82, 1-84, 1-98, 1-102, 1-103, 1-132, 1-133, 1-134, 1-138, 1-139, 1-140, 2-1, 2-2, 2-3, 2-4, 2-5, 2-6, 2-15, 2-16, 2-17, 2-18, 2-19, 2-20, 2-21, 2-22, 2-23, 2-24, 2-25, 2-26, 2-27, 2-28, 2-29, 2-30, 2-31, 2-32, 2-37, 2-38, 2-39, 2-40, 2-49, 2-50, 2-64, 2-65, 2-66, 2-67, 2-68, 2-69, 2-70, 2-71, 2-73, 2-74, 2-75, 2-76, 2-77, 3-1, 3-9, 3-10, 3-13, 3-14, 3-25, 3-26, 3-27, 3-35, 3-36, 3-39, 3-40, 3-51, 3-52, 3-53, 3-61, 3-65, 3-77, 3-78, 3-79, 3-87, 3-91, 3-103, 3-104, 3-105, 3-107, 3-109, 3-111, 3-112, 3-121, 3-127, 3-128, 3-129, 3-135, 3-136, 4-1, 4-4, 4-5, 4-6, 4-7, 4-8, 4-9, 4-10, 4-11, 4-14, 4-15, 4-16, 4-17, 4-18, 4-19, 4-20, 4-21, 4-22, 4-23, 4-25, 4-26, 4-27, 4-29, 4-31, 4-32, 4-33, 4-34, 4-35, 4-36, 4-38, 4-39, 4-41, 4-43, 4-44, 4-46, 4-49, 4-50, 4-51, 4-52, 4-53, 4-54, 4-55, 4-56, 4-59, 4-60, 4-61, 4-62, 4-63, 4-64, 4-65, 4-66, 4-67, 4-68, 4-70, 4-71, 4-72, 4-74, 4-76, 4-77, 4-78, 4-79, 4-80, 4-81, 4-83, 4-84, 4-85, 4-91, 4-96, 4-98, 4-99, 4-107, 4-109, 4-110, 4-112, 4-113, 4-114, 4-115, 5-1, 5-2, 5-3 , 5-5, 5-6, 5-13 , 5-14, 5-18, 5-19, 5-23, 5-24, 5-32, 5-33, 5-34, 5-36, 5-37, 5-44, 5-45, 5-49, 5-50, 5-54, 5-55, 5-63, 5-64, 5-65, 5-67, 5-68, 5-75, 5-76, 5-80, 5-81, 5-85, 5-86, 5-94, 5-95, 5-96, 5-98, 5-99, 5-106, 5-107, 5-111, 5-112, 5-116, 5-117, 5-125, 5-138, 5-151, 5-164, 5-177, 5-190, 5-203, 5-216, 5-229, 5-242, 5-255, 5-268, 5-281, 5-294, 5-307, 5-320, 5-348, 5-349, 5-350 and 5-351, of which Compounds No. 1-22, 1-25, 1-27, 1-28, 1-31, 1-35, 1-36, 1-37, 1-49, 1-54, 1-56, 1-58, 1-59, 1-132, 1-133, 1-134, 2-1, 2-2, 2-3, 2-5, 2-6, 2-15, 2-16, 2-17, 2-18, 2-19, 2-20, 2-21, 2-22, 2-23, 2-24, 2-25, 2-26, 2-27, 2-28, 2-29, 2-30, 2-31, 2-32, 2-65, 2-66, 2-67, 2-68, 2-69, 2-70, 2-71, 2-73, 2-74, 2-75, 2-76, 2-77, 3-1, 3-9, 3-10, 3-13, 3-14, 3-25, 3-26, 3-35, 3-39, 3-40, 3-52, 3-53 3-61, 3-65, 3-77, 3-78, 3-79, 3-87, 3-91, 3-103, 3-104, 3-105, 3-107, 3-109, 3-111, 3-112, 4-4, 4-5, 4-6, 4-7, 4-11, 4-14, 4-15, 4-16, 4-17, 4-20, 4-29, 4-31, 4-32, 4-33, 4-34, 4-35, 4-36, 4-38, 4-39, 4-41, 4-43, 4-44, 4-46, 4-49, 4-50, 4-51, 4-52, 4-55, 4-56, 4-59, 4-60, 4-61, 4-62, 4-65, 4-74, 4-76, 4-77, 4-78, 4-79, 4-80, 4-81, 4-83, 4-84, 4-91, 4-96, 4-107, 4-109, 4-110, 4-114, 4-115, 5-5, 5-6, 5-13, 5-14, 5-32, 5-36, 5-37, 5-44, 5-45, 5-63, 5-67, 5-68, 5-75, 5-76, 5-80, 5-81, 5-94, 5-98, 5-99, 5-106, 5-107, 5-348, 5-349, 5-350 and 5-351 are more preferred, and Compounds No. 1-28, 1-31, 1-35, 1-36, 1-49, 1-56, 1-58, 1-59, 1-132, 1-133, 1-134, 2-1, 2-2, 2-3, 2-5, 2-6, 2-15, 2-16, 2-17, 2-18, 2-19, 2-20, 2-21, 2-22, 2-23, 2-24, 2-25, 2-26, 2-27, 2-28, 2-29, 2-30, 2-31, 2-32, 2-65, 2-66, 2-67, 2-68, 2-69, 2-70, 2-71, 2-73, 2-74, 2-75, 2-76, 2-77, 3-1, 3-9, 3-10, 3-13, 3-14, 3-25, 3-26, 3-53, 3-61, 3-65, 3-77, 3-78, 4-29, 4-31, 4-32, 5-36 and 5-37 are still more preferred. The most preferred compounds are Compounds No.:

1-31. 2-Butyl-1-[(2'-carboxybiphenyl-4-yl)methyl]-4-(1-hydroxy-1-methylethyl)imidazole-5-carboxylic acid;

1-35. Pivaloyloxymethyl 2-butyl-1-[(2'-carboxybiphenyl-4-yl)methyl]-4-(1-hydroxy-1-methylethyl)imidazole-5-carboxylate;

1-36. (5-Methyl-2-oxo-1,3-dioxolen-4-yl)methyl 2-butyl-1-[(2'-carboxybiphenyl-4-yl)methyl]-4-(1-hydroxy-1-methylethyl)imidazole-5-carboxylate;

1-49. 1-[(2'-Carboxybiphenyl-4-yl)methyl]-4-(1-hydroxy-1-methylethyl)-2-propylimidazole-5-carboxylic acid;

1-132. 1-[(2'-Carboxybiphenyl-4-yl)methyl]-2-ethyl-4-(1-hydroxy-1-methylethyl)imidazole-5-carboxylic acid;

2-1. 4-(1-Hydroxy-1-methylethyl)-2-propyl-1-{4-[2-(tetrazol-5-yl)phenyl]phenyl}methylimidazole-5-carboxylic acid;

2-2. 2-Butyl -4-(1-hydroxy-1-methylethyl)-1-{4-[2-(tetrazol-5-yl)phenyl]phenyl}methylimidazole-5carboxylic acid;

2-15. Pivaloyloxymethyl 4-(1-hydroxy-1-methylethyl)-2-propyl-1-{4-[2-(tetrazol-5-yl)phenyl] phenyl}methylimidazole-5-carboxylate;

2-16. Pivaloyloxymethyl 2-butyl-4-(1-hydroxy-1-methylethyl)-1)-1-{4-[2-(tetrazol-5-yl)phenyl] phenyl}methylimidazole-5-carboxylate;

2-17. (5-Methyl-2-oxo-1,3-dioxolen-4-yl)methyl 4-(1-hydroxy-1-methylethyl)-2-propyl-1-{4-[2-(tetrazol-5-yl)phenyl]phenyl}methylimidazole-5-carboxylate;

2-18. (5-Methyl-2-oxo-1,3-dioxolen-4-yl)methyl 2-butyl-4-(1-hydroxy-1-methylethyl)-1-{4-[2-(tetrazol-5-yl)phenyl]phenyl}methylimidazole-5-carboxylate;

2-19. Ethoxycarbonyloxymethyl 4-(1-hydroxy-1-methylethyl)-2-propyl-1-{4-[2-(tetrazol-5-yl)phenyl]phenyl}-methylimidazole-5-carboxylate;

2-21. Isopropoxycarbonyloxymethyl 4-(1-hydroxy-1methylethyl)-2-propyl-1-{4-[2-(tetrazol-5-yl)phenyl] phenyl}methylimidazole-5-carboxylate;

2-23. 1-(Ethoxycarbonyloxy)ethyl 4-(1-hydroxy-1-methylethyl)-2-propyl-1-{4-[2-(tetrazol-5-yl)phenyl]phenyl}-methylimidazole-5-carboxylate;

2-25. 1-(Isopropoxycarbonyloxy)ethyl-(1-hydroxy-1-methylethyl)-2-propyl-1-{4-[2-(tetrazol-5-yl)phenyl] phenyl}methylimidazole-5-carboxylate;

2-69. Pivaloyloxymethyl 2-ethyl-4-(1-hydroxy-1-methylethyl)-1-{4-[2-(tetrazol-5-yl)phenyl] phenyl}methylimidazole-5-carboxylate;

2-73. (5-Methyl-2-oxo-1,3-dioxolen-4-yl)methyl 2-ethyl-4-(1-hydroxy-1-methylethyl)-1-{4-[2-(tetrazol-5-yl)phenyl]phenyl}methylimidazole-5-carboxylate;

3-1. Pivaloyloxymethyl 1-{(2'-carboxybiphenyl-4-yl)methyl]-4-(1-hydroxy-1-methylethyl)-2-propylimidazole-5-carboxylate;

3-25. (5-Methyl -2-oxo-1,3-dioxolen-4-yl)methyl 1-[(2'-carboxybiphenyl-4-yl)methyl]-4-(1-hydroxy-1-methylethyl)-2-propylimidazole-5-carboxylate;

3-26. Phthalidyl 1-[(2'-carboxybiphenyl-4-yl)methyl]-4-(1-hydroxy-1-methylethyl)-2-propylimidazole-5-carboxylate;

4-29. 4-(1-Hydroxyethyl)-2-propyl-1-{4-[2-(tetrazol-5-yl)phenyl]phenyl}methylimidazole-5-carboxylic acid;

4-31. Pivaloyloxymethyl 4-(1-hydroxyethyl)-2-propyl-1-{4-[2-(tetrazol-5-yl)phenyl]phenyl}methylimidazole-5-carboxylate; and

4-32. (5-Methyl-2-oxo-1,3-dioxolen-4-yl)methyl 4-(1-hydroxyethyl)-2-propyl-1-{4-[2-(tetrazol-5-yl)phenyl] phenyl}methylimidazole-5-carboxylate;

and pharmaceutically acceptable salts thereof.

Specific examples of compounds of formula $(Ia)_p$, shown above, in which R_p^1—X_p—R_p^2—, R_p^3, R_p^4, R_p^5 and R_p^6 are

as defined in the following Table 7. In the Table 7, the following abbreviations are employed:

Bu	butyl
Et	ethyl
Etc	ethoxycarbonyl
Me	methyl
Mod	(5-methyl-2-oxo-1,3-dioxolen-4-yl)methyl
Phth	3-phthalidyl
Pom	pivaloyloxymethyl
Pr	Propyl
iPr	isopropyl
iPrc	isopropoxycarbonyl
Tz	tetrazol-5-yl

TABLE 7

Compound No.	R_p^1-X_p-R_p^2-	R_p^3	R_p^4	R_p^5	R_p^6
1	$MeOCH_2$—	Me	Me	H	COOH
2	$MeOCH_2$—	Me	Me	H	Tz
3	$EtOCH_2$—	Me	Me	H	COOH
4	$EtOCH_2$—	Me	Me	H	Tz
5	$PrOCH_2$—	Me	Me	H	COOH
6	$PrOCH_2$—	Me	Me	H	Tz
7	$BuOCH_2$—	Me	Me	H	COOH
8	$BuOCH_2$—	Me	Me	H	Tz
9	$iPrOCH_2$—	Me	Me	H	COOH
10	$iPrOCH_2$—	Me	Me	H	Tz
11	1-(MeO)Et	Me	Me	H	COOH
12	1-(MeO)Et	Me	Me	H	Tz
13	2-(MeO)Et	Me	Me	H	COOH
14	2-(MeO)Et	Me	Me	H	Tz
15	2-(EtO)Et	Me	Me	H	COOH
16	2-(EtO)Et	Me	Me	H	Tz
17	$MeSCH_2$—	Me	Me	H	COOH
18	$MeSCH_2$—	Me	Me	H	Tz
19	$EtSCH_2$—	Me	Me	H	COOH
20	$EtSCH_2$—	Me	Me	H	Tz
21	1-(MeS)Et	Me	Me	H	COOH
22	1-(MeS)Et	Me	Me	H	Tz
23	MeS—	Me	Me	H	COOH
24	MeS—	Me	Me	H	Tz
25	EtS—	Me	Me	H	COOH
26	EtS—	Me	Me	H	Tz
27	PrS—	Me	Me	H	COOH
28	PrS—	Me	Me	H	Tz
29	$MeOCH_2$—	Me	Et	H	COOH
30	$MeOCH_2$—	Me	Et	H	Tz
31	$EtOCH_2$—	Me	Et	H	COOH
32	$EtOCH_2$—	Me	Et	H	Tz
33	$PrOCH_2$—	Me	Et	H	COOH
34	$PrOCH_2$—	Me	Et	H	Tz
35	$BuOCH_2$—	Me	Et	H	COOH
36	$BuOCH_2$—	Me	Et	H	Tz
37	$iPrOCH_2$—	Me	Et	H	COOH
38	$iPrOCH_2$—	Me	Et	H	Tz
39	1-(MeO)Et	Me	Et	H	COOH
40	1-(MeO)Et	Me	Et	H	Tz
41	2-(MeO)Et	Me	Et	H	COOH
42	2-(MeO)Et	Me	Et	H	Tz
43	2-(EtO)Et	Me	Et	H	COOH
44	2-(EtO)Et	Me	Et	H	Tz
45	$MeSCH_2$—	Me	Et	H	COOH
46	$MeSCH_2$—	Me	Et	H	Tz
47	$EtSCH_2$—	Me	Et	H	COOH
48	$EtSCH_2$—	Me	Et	H	Tz
49	1-(MeS)Et	Me	Et	H	COOH
50	1-(MeS)Et	Me	Et	H	Tz
51	MeS—	Me	Et	H	COOH
52	MeS—	Me	Et	H	Tz
53	EtS—	Me	Et	H	COOH
54	EtS—	Me	Et	H	Tz
55	PrS—	Me	Et	H	COOH
56	PrS—	Me	Et	H	Tz
57	$MeOCH_2$—	Et	Et	H	COOH
58	$MeOCH_2$—	Et	Et	H	Tz

TABLE 7-continued

Compound No.	R_p^1-X_p-R_p^2-	R_p^3	R_p^4	R_p^5	R_p^6
59	$EtOCH_2$—	Et	Et	H	COOH
60	$EtOCH_2$—	Et	Et	H	Tz
61	$PrOCH_2$—	Et	Et	H	COOH
62	$PrOCH_2$—	Et	Et	H	Tz
63	$BuOCH_2$—	Et	Et	H	COOH
64	$BuOCH_2$—	Et	Et	H	Tz
65	$iPrOCH_2$—	Et	Et	H	COOH
66	$iPrOCH_2$—	Et	Et	H	Tz
67	1-(MeO)Et	Et	Et	H	COOH
68	1-(MeO)Et	Et	Et	H	Tz
69	2-(MeO)Et	Et	Et	H	COOH
70	2-(Meo)Et	Et	Et	H	Tz
71	2-(Eto)Et	Et	Et	H	COOH
72	2-(EtO)Et	Et	Et	H	Tz
73	$MeSCH_2$—	Et	Et	H	COOH
74	$MeSCH_2$—	Et	Et	H	Tz
75	$EtSCH_2$—	Et	Et	H	COOH
76	$EtSCH_2$—	Et	Et	H	Tz
77	1-(MeS)Et	Et	Et	H	COOH
78	1-(MeS)Et	Et	Et	H	Tz
79	MeS—	Et	Et	H	COOH
80	MeS—	Et	Et	H	Tz
81	EtS—	Et	Et	H	COOH
82	EtS—	Et	Et	H	Tz
83	PrS—	Et	Et	H	COOH
84	PrS—	Et	Et	H	Tz
85	$MeOCH_2$—	Me	Me	Pom	COOH
86	$MeOCH_2$—	Me	Me	Pom	Tz
87	$EtOCH_2$—	Me	Me	Pom	COOH
88	$EtOCH_2$—	Me	Me	Pom	Tz
89	$MeSCH_2$—	Me	Me	Pom	COOH
90	$MeSCH_2$—	Me	Me	Pom	Tz
91	MeS—	Me	Me	Pom	COOH
92	MeS—	Me	Me	Pom	Tz
93	EtS—	Me	Me	Pom	COOH
94	EtS—	Me	Me	Pom	Tz
95	$MeOCH_2$—	Me	Me	Mod	COOH
96	$MeOCH_2$—	Me	Me	Mod	Tz
97	$EtOCH_2$—	Me	Me	Mod	COOH
98	$EtOCH_2$—	Me	Me	Mod	Tz
99	$MeSCH_2$—	Me	Me	Mod	COOH
100	$MeSCH_2$—	Me	Me	Mod	Tz
101	MeS—	Me	Me	Mod	COOH
102	MeS—	Me	Me	Mod	Tz
103	EtS—	Me	Me	Mod	COOH
104	EtS—	Me	Me	Mod	Tz
105	$MeOCH_2$—	Me	Me	$EtcOCH_2$—	COOH
106	$MeOCH_2$—	Me	Me	$EtcOCH_2$—	Tz
107	$EtOCH_2$—	Me	Me	$EtcOCH_2$—	COOH
108	$EtOCH_2$—	Me	Me	$EtcOCH_2$—	Tz
109	$MeSCH_2$—	Me	Me	$EtcOCH_2$—	COOH
110	$MeSCH_2$—	Me	Me	$EtcOCH_2$—	Tz
111	MeS—	Me	Me	$EtcOCH_2$—	COOH
112	MeS—	Me	Me	$EtcOCH_2$—	Tz
113	EtS—	Me	Me	$EtcOCH_2$—	COOH
114	EtS—	Me	Me	$EtcOCH_2$—	Tz
115	$MeOCH_2$—	Me	Me	$iPrcOCH_2$—	COOH
116	$MeOCH_2$—	Me	Me	$iPrcOCH_2$—	Tz
117	$EtOCH_2$—	Me	Me	$iPrcOCH_2$—	COOH
118	$EtOCH_2$—	Me	Me	$iPrcOCH_2$—	Tz
119	$MeSCH_2$—	Me	Me	$iPrcOCH_2$—	COOH
120	$MeSCH_2$—	Me	Me	$iPrcOCH_2$—	Tz
121	MeS—	Me	Me	$iPrcOCH_2$—	COOH
122	MeS—	Me	Me	$iPrcOCH_2$—	Tz
123	EtS—	Me	Me	$iPrcOCH_2$—	COOH
124	EtS—	Me	Me	$iPrcOCH_2$—	Tz
125	$MeOCH_2$—	Me	Me	1-(EtcO)Et	COOH
126	$MeOCH_2$—	Me	Me	1-(EtcO)Et	Tz
127	$EtOCH_2$—	Me	Me	1-(EtcO)Et	COOH
128	$EtOCH_2$—	Me	Me	1-(EtcO)Et	Tz
129	$MeSCH_2$—	Me	Me	1-(EtcO)Et	COOH
130	$MeSCH_2$—	Me	Me	1-(EtcO)Et	Tz
131	MeS—	Me	Me	1-(EtcO)Et	COOH
132	MeS—	Me	Me	1-(EtcO)Et	Tz
133	EtS—	Me	Me	1-(EtcO)Et	COOH
134	EtS—	Me	Me	1-(EtcO)Et	Tz

TABLE 7-continued

Compound No.	R_p^1-X_p-R_p^2-	R_p^3	R_p^4	R_p^5	R_p^6
135	$MeOCH_2$—	Me	Me	1-(iPrcO)Et	COOH
136	$MeOCH_2$—	Me	Me	1-(iPrcO)Et	Tz
137	$EtOCH_2$—	Me	Me	1-(iPrcO)Et	COOH
138	$EtOCH_2$—	Me	Me	1-(iPrcO)Et	Tz
139	$MeSCH_2$—	Me	Me	1-(iPrcO)Et	COOH
140	$MeSCH_2$—	Me	Me	1-(iPrcO)Et	Tz
141	MeS—	Me	Me	1-(iPrcO)Et	COOH
142	MeS—	Me	Me	1-(iPrcO)Et	Tz
143	EtS—	Me	Me	1-(iPrcO)Et	COOH
144	EtS—	Me	Me	1-(iPrcO)Et	Tz
145	$MeOCH_2$—	Me	Me	Phth	COOH
146	$MeOCH_2$—	Me	Me	Phth	Tz
147	$EtOCH_2$—	Me	Me	Phth	COOH
148	$EtOCH_2$—	Me	Me	Phth	Tz
149	$MeSCH_2$—	Me	Me	Phth	COOH
150	MeS—	Me	Me	Phth	Tz
151	MeS—	Me	Me	Phth	COOH
152	MeS—	Me	Me	Phth	Tz
153	EtS—	Me	Me	Phth	COOH
154	EtS—	Me	Me	Phth	Tz
155	$MeOCH_2$—	Me	Me	Me	COOH
156	$MeOCH_2$—	Me	Me	Me	Tz
157	$EtOCH_2$—	Me	Me	Et	COOH
158	$EtOCH_2$—	Me	Me	Et	Tz
159	$PrOCH_2$—	Me	Me	Pr	COOH
160	$PrOCH_2$—	Me	Me	Pr	Tz
161	$iPrOCH_2$—	Me	Me	iPr	COOH
162	$iPrOCH_2$—	Me	Me	iPr	Tz
163	1-(MeO)Et	Me	Me	Me	COOH
164	1-(MeO)Et	Me	Me	Me	Tz
165	$MeSCH_2$—	Me	Me	Et	COOH
166	$MeSCH_2$—	Me	Me	Et	Tz
167	MeS—	Me	Me	Et	COOH
168	MeS—	Me	Me	Et	Tz
169	EtS—	Me	Me	Et	COOH
170	EtS—	Me	Me	Et	Tz
171	PrS—	Me	Me	Et	COOH
172	PrS—	Me	Me	Et	Tz
173	1-(EtO)Et	Me	Me	H	COOH
174	1-(EtO)Et	Me	Me	H	Tz
175	1-(EtO)Et	Me	Me	Pom	COOH
176	1-(EtO)Et	Me	Me	Pom	Tz
177	1-(EtO)Et	Me	Me	Mod	COOH
178	1-(Eto)Et	Me	Me	Mod	Tz
179	1-(EtO)Et	Me	Me	Et	COOH
180	1-(EtO)Et	Me	Me	Et	Tz
181	$HOCH_2$—	Me	Me	H	COOH
182	$HOCH_2$—	Me	Me	H	Tz
183	$HOCH_2$—	Me	Me	Et	COOH
184	$HOCH_2$—	Me	Me	Et	Tz
185	$MeOCH_2$—	Me	Et	Pom	COOH
186	$MeOCH_2$—	Me	Et	Pom	Tz
187	$MeSCH_2$—	Me	Et	Pom	COOH
188	$MeSCH_2$—	Me	Et	Pom	Tz
189	MeS—	Me	Et	Pom	COOH
190	MeS—	Me	Et	Pom	Tz
191	$MeOCH_2$—	Me	Et	Mod	COOH
192	$MeOCH_2$—	Me	Et	Mod	Tz
193	$MeSCH_2$—	Me	Et	Mod	COOH
194	$MeSCH_2$—	Me	Et	Mod	Tz
195	MeS—	Me	Et	Mod	COOH
196	MeS—	Me	Et	Mod	Tz
197	EtS—	Me	Et	Mod	COOH
198	EtS—	Me	Et	Mod	Tz
199	$MeOCH_2$—	Me	Et	$EtcOCH_2$—	COOH
200	$MeOCH_2$—	Me	Et	$EtcOCH_2$—	Tz
201	$MeSCH_2$—	Me	Et	$EtcOCH_2$—	COOH
202	$MeSCH_2$—	Me	Et	$EtcOCH_2$—	Tz
203	MeS—	Me	Et	$EtcOCH_2$—	COOH
204	MeS—	Me	Et	$EtcOCH_2$—	Tz
205	$MeOCH_2$—	Me	Et	$iPrcOCH_2$—	COOH
206	$MeOCH_2$—	Me	Et	$iPrcOCH_2$—	Tz
207	$MeSCH_2$—	Me	Et	$iPrcOCH_2$—	COOH
208	$MeSCH_2$—	Me	Et	$iPrcOCH_2$—	Tz
209	MeS—	Me	Et	$iPrcOCH_2$—	COOH
210	MeS—	Me	Et	$iPrcOCH_2$—	Tz

TABLE 7-continued

Compound No.	R_p^1-X_p-R_p^2-	R_p^3	R_p^4	R_p^5	R_p^6
211	EtS—	Me	Et	$iPrcOCH_2$—	Tz
212	$MeOCH_2$—	Me	Et	1-(EtcO)Et	COOH
213	$MeOCH_2$—	Me	Et	1-(EtcO)Et	Tz
214	$MeSCH_2$—	Me	Et	1-(EtcO)Et	COOH
215	$MeSCH_2$—	Me	Et	1-(EtcO)Et	Tz
216	MeS—	Me	Et	1-(EtcO)Et	COOH
217	MeS—	Me	Et	1-(EtcO)Et	Tz
218	$MeOCH_2$—	Me	Et	1-(iPrcO)Et	COOH
219	$MeOCH_2$—	Me	Et	1-(iPrcO)Et	Tz
220	$MeSCH_2$—	Me	Et	1-(iPrcO)Et	COOH
221	$MeSCH_2$—	Me	Et	1-(iPrcO)Et	Tz
222	MeS—	Me	Et	1-(iPrcO)Et	COOH
223	MeS—	Me	Et	1-(iPrcO)Et	Tz
224	$MeOCH_2$—	Me	Et	Phth	COOH
225	$MeOCH_2$—	Me	Et	Phth	Tz
226	$MeSCH_2$—	Me	Et	Phth	COOH
227	$MeSCH_2$—	Me	Et	Phth	Tz
228	MeS—	Me	Et	Phth	COOH
229	MeS—	Me	Et	Phth	Tz
230	$MeOCH_2$—	Me	H	H	COOH
231	$MeOCH_2$—	Me	H	H	Tz
232	$EtOCH_2$—	Me	H	H	COOH
233	$EtOCH_2$—	Me	H	H	Tz
234	1-(MeO)Et	Me	H	H	COOH
235	1-(MeO)Et	Me	H	H	Tz
236	$MeSCH_2$—	Me	H	H	COOH
237	$MeSCH_2$—	Me	H	H	Tz
238	$EtSCH_2$—	Me	H	H	COOH
239	$EtSCH_2$—	Me	H	H	Tz
240	1-(MeS)Et	Me	H	H	COOH
241	1-(MeS)Et	Me	H	H	Tz
242	MeS—	Me	H	H	COOH
243	MeS—	Me	H	H	Tz
244	EtS—	Me	H	H	COOH
245	EtS—	Me	H	H	Tz
246	$MeOCH_2$—	Me	H	Pom	COOH
247	$MeOCH_2$—	Me	H	Pom	Tz
248	$MeSCH_2$—	Me	H	Pom	COOH
249	$MeSCH_2$—	Me	H	Pom	Tz
250	MeS—	Me	H	Pom	COOH
251	MeS—	Me	H	Pom	Tz
252	$MeOCH_2$—	Me	H	Mod	COOH
253	$MeOCH_2$—	Me	H	Mod	Tz
254	$MeSCH_2$—	Me	H	Mod	COOH
255	$MeSCH_2$—	Me	H	Mod	Tz
256	MeS—	Me	H	Mod	COOH
257	MeS—	Me	H	Mod	Tz
258	EtS—	Me	H	Mod	COOH
259	EtS—	Me	H	Mod	Tz
260	$MeOCH_2$—	Me	H	$EtcOCH_2$—	Tz
261	$MeSCH_2$—	Me	H	$EtcOCH_2$—	COOH
262	$MeSCH_2$—	Me	H	$EtcOCH_2$—	Tz
263	MeS—	Me	H	$EtcOCH_2$—	Tz
264	$MeOCH_2$—	Me	H	$iPrcOCH_2$—	COOH
265	$MeOCH_2$—	Me	H	$iPrcOCH_2$—	Tz
266	$MeSCH_2$—	Me	H	$iPrcOCH_2$—	COOH
267	$MeSCH_2$—	Me	H	$iPrcOCH_2$—	Tz
268	MeS—	Me	H	$iPrcOCH_2$—	COOH
269	MeS—	Me	H	$iPrcOCH_2$—	Tz
270	$MeOCH_2$—	Me	H	1-(EtcO)Et	Tz
271	$MeSCH_2$—	Me	H	1-(EtcO)Et	COOH
272	$MeSCH_2$—	Me	H	1-(EtcO)Et	Tz
273	MeS—	Me	H	1-(EtcO)Et	COOH
274	MeS—	Me	H	1-(EtcO)Et	Tz
275	$MeOCH_2$—	Me	H	1-(iPrcO)Et	Tz
276	$MeSCH_2$—	Me	H	1-(iPrcO)Et	Tz
277	MeS—	Me	H	1-(iPrcO)Et	Tz
278	$MeOCH_2$—	Me	H	Phth	Tz
279	$MeSCH_2$—	Me	H	Phth	Tz
280	MeS—	Me	H	Phth	COOH
281	MeS—	Me	H	Phth	Tz
282	$MeOCH_2$—	H	H	H	Tz
283	$EtOCH_2$—	H	H	H	COOH
284	$EtOCH_2$—	H	H	H	Tz
285	1-(MeO)Et	H	H	H	Tz
286	$MeSCH_2$—	H	H	H	COOH

TABLE 7-continued

Compound No.	R_p^1-X_p-R_p^2-	R_p^3	R_p^4	R_p^5	$R_p^{6'}$
287	$MeSCH_2$—	H	H	H	Tz
288	$EtSCH_2$—	H	H	H	COOH
289	$EtSCH_2$—	H	H	H	Tz
290	1-(MeS)Et	H	H	H	COOH
291	1-(MeS)Et	H	H	H	Tz
292	MeS—	H	H	H	COOH
293	MeS—	H	H	H	Tz
294	EtS—	H	H	H	COOH
295	EtS—	H	H	H	Tz
296	$MeOCH_2$—	H	H	Pom	Tz
297	$MeSCH_2$—	H	H	Pom	COOH
298	$MeSCH_2$—	H	H	Pom	Tz
299	MeS—	H	H	Pom	Tz
300	$MeOCH_2$—	H	H	Mod	COOH
301	$MeOCH_2$—	H	H	Mod	Tz
302	$MeSCH_2$—	H	H	Mod	COOH
303	$MeSCH_2$—	H	H	Mod	Tz
304	MeS—	H	H	Mod	COOH
305	MeS—	H	H	Mod	Tz
306	EtS—	H	H	Mod	COOH
307	EtS—	H	H	Mod	Tz
308	$MeOCH_2$—	H	H	$EtcOCH_2$—	Tz
309	$MeSCH_2$—	H	H	$EtcOCH_2$—	Tz
310	MeS—	H	H	$EtcOCH_2$—	Tz
311	$MeOCH_2$—	H	H	$iPrcOCH_2$—	Tz
312	$MeSCH_2$—	H	H	$iPrcOCH_2$—	Tz
313	MeS—	H	H	$iPrcOCH_2$—	Tz
314	$MeOCH_2$—	H	H	1-(EtcO)Et	Tz
315	$MeSCH_2$—	H	H	1-(EtcO)Et	Tz
316	MeS—	H	H	1-(EtcO)Et	Tz
317	$MeOCH_2$—	H	H	1-(iPrcO)Et	Tz
318	$MeSCH_2$—	H	H	1-(iPrcO)Et	Tz
319	MeS—	H	H	1-(iPrcO)Et	Tz
320	$MeOCH_2$—	H	H	Phth	Tz
321	$MeSCH_2$—	H	H	Phth	Tz
322	MeS—	H	H	Phth	COOH
323	MeS—	H	H	Phth	Tz
324	$EtOCH_2$—	Me	H	Pom	COOH
325	$EtOCH_2$—	Me	H	Pom	Tz
326	$EtOCH_2$—	Me	H	Mod	COOH
327	$EtOCH_2$—	Me	H	Mod	Tz
328	$EtOCH_2$—	Me	H	$EtcOCH_2$—	COOH
329	$EtOCH_2$—	Me	H	$EtcOCH_2$—	Tz
330	$EtOCH_2$—	Me	H	$iPrcOCH_2$—	COOH
331	$EtOCH_2$—	Me	H	$iPrcOCH_2$—	Tz
332	$EtOCH_2$—	Me	H	1-(iPrcO)Et	COOH
333	$EtOCH_2$—	Me	H	1-(iPrcO)Et	Tz
334	$EtOCH_2$—	Me	H	Phth	COOH
335	$EtOCH_2$—	Me	H	Phth	Tz
336	$EtOCH_2$—	H	H	Pom	COOH
337	$EtOCH_2$—	H	H	$EtcOCH_2$—	Tz
338	$EtOCH_2$—	H	H	1-(EtcO)Et	Tz
339	$EtOCH_2$—	H	H	Phth	Tz
340	$MeOCH_2$—	H	H	H	COOH

Of the compounds illustrated above, preferred compounds are Compounds No. 1, 2, 3, 4, 5, 6, 9, 10, 11, 12, 17, 18, 19, 20, 23, 24, 25, 26, 27, 28, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 230, 231, 232, 233, 236, 237, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273,274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 286, 287, 288, 289, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315, 316, 317, 318, 319, 320, 321, 322, 323, 324, 325, 326, 327, 328, 329, 330, 331, 332, 333, 334, 335, 336, 337, 338, 339 and 340; and more preferred compounds are Compounds No. 1, 2, 3, 4, 17, 18, 19, 20, 23, 24, 25, 26,

85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 231, 233, 247, 253, 260, 265, 270, 275, 278, 282, 284, 296, 301, 308, 311, 314, 317, 320, 325, 327, 329, 331, 333, 335, 337, 338 and 339.

The most preferred specific compounds are Compounds No.:

2. 4-(1-hydroxy-1-methylethyl)-2-methoxymethyl-1-{4-[2-(tetrazol-5-yl)phenyl]phenyl}methylimidazole-5-carboxylic acid;

4. 2-ethoxymethyl-4-(1-hydroxy-1-methylethyl)-1-{4-[2-(tetrazol-5-yl)phenyl]phenyl}methylimidazole-5-carboxylic acid;

26. 2-ethylthio-4-(1-hydroxy-1-methylethyl)-1-{4-[2-(tetrazol-5-yl)phenyl]phenyl}methylimidazole-5-carboxylic acid;

86. pivaloyloxymethyl 4-(1-hydroxy-1-methylethyl)-2-methoxymethyl-1-{4-[2-(tetrazol-5-yl)phenyl]phenyl}-methylimidazole-5-carboxylate;

88. pivaloyloxymethyl 2-ethoxymethyl-4-(1-hydroxy-1-methylethyl)-1-{4-[2-(tetrazol-5-yl)phenyl] phenyl}methylimidazole-5-carboxylate;

94. pivaloyloxymethyl 2-ethylthio-4-(1-hydroxy-1-methylethyl)-1-{4-[2-(tetrazol-5-yl)phenyl] phenyl}methylimidazole-5-carboxylate;

96. (5-methyl-2-oxo-1,3-dioxolen-4-yl)methyl 4-(1-hydroxy-1-methylethyl)-2-methoxymethyl-1-{4-[2-(tetrazol-5-yl)phenyl]phenyl}methylimidazole-5-carboxylate;

98. (5-methyl-2-oxo-1,3-dioxolen-4-yl)methyl 2-ethoxymethyl-4-(1-hydroxy-1-methylethyl)-1-{4-[2-(tetrazol-5-yl)phenyl]phenyl}methylimidazole-5-carboxylate;

104. (5-methyl-2-oxo-1,3-dioxolen-4-yl)methyl 2-ethylthio-4-(1-hydroxy-1-methylethyl)-1-{4-[2-(tetrazol-5-yl)phenyl]phenyl}methylimidazole-5-carboxylate;

106. ethoxycarbonyloxymethyl 4-(1-hydroxy-1-methylethyl)-2-methoxymethyl-1-{4-[2-(tetrazol-5-yl)phenyl] phenyl}methylimidazole-5-carboxylate;

108. ethoxycarbonyloxymethyl 2-ethoxymethyl-4-(1-hydroxy-1-methylethyl)-1-{4-[2-(tetrazol-5-yl)phenyl] phenyl}methylimidazole-5-carboxylate;

114. ethoxycarbonyloxymethyl 2-ethylthio-4-(1-hydroxy-1-methylethyl)-1-{4-[2-(tetrazol-5-yl)phenyl] phenyl}methylimidazole-5-carboxylate;

116. isopropoxycarbonylmethyl 4-(1-hydroxy-1-methylethyl)-2-methoxymethyl-1-{4-[2-(tetrazol-5-yl)phenyl] phenyl}methylimidazole-5-carboxylate;

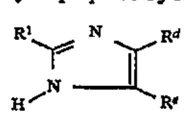
118. isopropoxycarbonyloxxymethyl 2-ethoxymethyl-4-(1-hydroxy-1-methylethyl)-1-{4-[2-(tetrazol-5-yl)phenyl] phenyl}methylimidazole-5-carboxylate and;

124. isopropoxycarbonyloxymethyl 2-ethylthio-4-(1-hydroxy-1-methylethyl)-1-{4- [2-(tetrazol-5-yl)phenyl] phenyl}methylimidazole-5-carboxylate;

and pharmaceutically acceptable salts and esters thereof.

The compounds of formula (I) of the present invention can be prepared by a variety of methods well known in the art for the preparation of compounds of this type.

The example, in general terms, the compounds of formula (I) may be prepared by reacting a compound of formula (II):



(II)

in which:

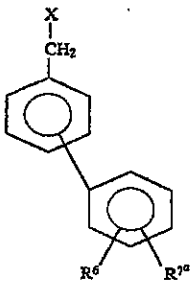
R^1 is as defined above and R^d represents a group of formula

wherein R^2, R^3 and R^4 are as defined above,

or R^d represents a group of formula —$COOR^f$ wherein R^f represents a carboxy-protecting group, R^d represents a group of formula —COR^2, wherein R^2 is as defined above or R^d represents a cyano group; and

R^e represents a cyano group, a carboxy group or a group of formula —$COOR^f$, wherein R^f is as defined above,

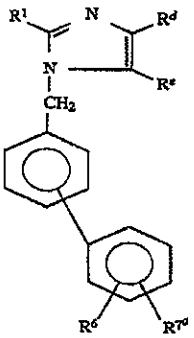
with a compound of formula (III):



(III)

in which: R^6 is as defined above; R^{7a} represents a protected carboxy group, a cyano group, a protected tetrazol-5-yl group, a carbamoyl group or an alkylcarbamoyl group; and X represents a halogen atom;

to give a compound of formula (IV):



(IV)

wherein R^d, R^e, R^1, R^6 and R^{7a} are as defined above; and in any order, removing protecting groups, and, if necessary, converting said group R^d to a group of formula

wherein R^2, R^3 and R^4 are as defined above,

and, if necessary, converting said group R^e to a group R^5, converting said group R^{7a} to a group R^7, or alkylating or acylating a hydroxy group in R^4, to give a compound of formula (I); and

optionally salifying or esterifying the product.

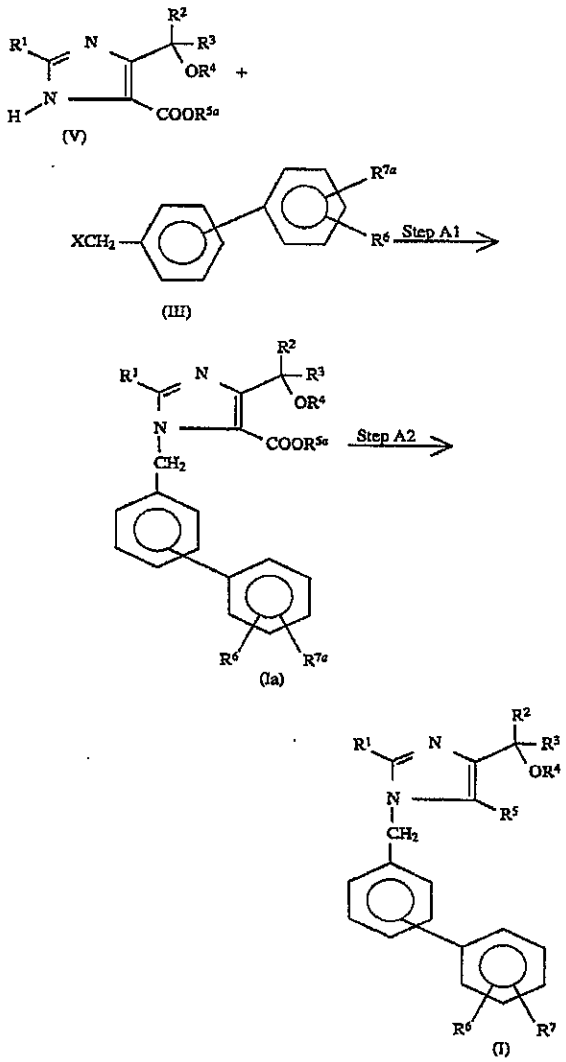
Preferably, R^e represents a protected carboxy group, when R^{7a} represents a protected carboxy group, a cyano group, a protected tetrazolyl group, a carbamoyl group or an alkylcarbamoyl group, and R^e represents a cyano group when R^{7a} represents a protected carboxy group or a protected tetrazolyl group.

In more detail, the compounds of formula (I) of the present invention may be prepared as described below in Reaction Schemes A to F.

Reaction Scheme A:

In this Reaction Scheme, a compound of formula (I) is prepared by reacting an imidazole-5-carboxylic acid or ester thereof of formula (V) with a biphenylmethyl halide of formula (III), and then, if desired, removing protecting groups, converting the group of formula —$COOR^{5a}$ to any other group represented by R^5, converting the group represented by R^{7a} to any other group represented by R^7 and/or alkylating or acylating a hydroxy group in R^4, as shown below:

Reaction Scheme A:



In the above reaction scheme, R^1, R^2, R^3, R^4, R^5, R^{5a}, R^6, R^7, R^{7a} and X are as defined above, and R^{5a} preferably represents a group other than a hydrogen atom.

Where R^{7a} represents a protected carboxy group, the protecting group may be any of the ester residues illustrated above in relation to R^{5a}. Alternatively, R^{7a} may be a carbamoyl group or a substituted carbamoyl group of formula —CONHR, where R represents a hydrogen atom or an alkyl group having from 1 to 6 carbon atoms, for example any of those illustrated above in relation to R^1. Examples of such carbamoyl groups which may be represented by R^{7a} include the carbamoyl, methylcarbamoyl, ethylcarbamoyl, propylcarbamoyl, butylcarbamoyl, t-butylcarbamoyl, pentylcarbamoyl, t-pentylcarbamoyl and hexylcarbamoyl groups, of which the carbamoyl, t-butylcarbamoyl and t-pentylcarbamoyl groups are preferred. Where R^{7a} represents a protected tetrazolyl group, the protecting group may be any protecting group commonly used to protect tetrazolyl groups in conventional compounds of this type. Examples of suitable protecting groups include the aralkyl groups defined and exemplified above in relation to R^2, but is preferably a benzyl, diphenylmethyl (benzhydryl) or triphenylmethyl (trityl group), most preferably a trityl group.

X represents a halogen atom, preferably a chlorine, bromine or iodine atom).

In Step A1 of this Reaction Scheme, a compound of formula (Ia) is prepared by reacting an imidazole-5-carboxylate compound of formula (V) with a biphenylmethyl compound of formula (III). The reaction normally and preferably takes place in an inert solvent and preferably in the presence of a base.

The reaction is normally and preferably effected in the presence of a solvent. There is no particular restriction on the nature of the solvent to be employed, provided than it has no adverse effect on the reaction or on the reagents involved and that it can dissolve the reagents, at least to some extent. Examples of suitable solvents include: hydrocarbons, preferably aromatic hydrocarbons, such as benzene or toluene; ethers, such as tetrahydrofuran or dioxane; alcohols, such as methanol, ethanol or t-butanol; amides, such as N,N-dimethylacetamide, N,N-dimethylformamide or N-methyl-2-pyrrolidinone; ketones, such as acetone or methyl ethyl ketone; nitriles, such as acetonitrile; and sulfoxides, such as dimethyl sulfoxide. Of these, we prefer the amides, ketones, nitriles and sulfoxides.

The nature of the base employed in the reaction is likewise not critical, and any base capable of reacting with the acid H-X can be used in this reaction. Preferred examples of bases which may be used include: alkali metal carbonates, such as sodium carbonate or potassium carbonate; alkali metal hydrides, such as sodium hydride, potassium hydride or lithium hydride; alkali metal alkoxides, such as sodium methoxide, sodium ethoxide, potassium t-butoxide or lithium methoxide; and alkali metal bicarbonates, such as sodium bicarbonate or potassium bicarbonate. Of these, we prefer the alkali metal carbonates, alkali metal hydrides or alkali metal alkoxides.

The reaction can take place over a wide range of temperatures, and the precise reaction temperature is not critical to the invention. In general, we find it convenient to carry out the reaction at a temperature of from —10° C. to 100° C., more preferably from 0° C. to 80° C. The time required for the reaction may also vary widely, depending on many factors, notably the reaction temperature and the nature of the reagents and solvent employed. However, provided that the reaction is effected under the preferred conditions outlined above, a period of from 30 minutes to 24 hours, more preferably from 1 to 16 hours, will usually suffice.

After completion of the reaction, the desired compound of formula (Ia) can be recovered from the reaction mixture by conventional means. For example, one suitable recovery procedure comprises: removing the solvent by distillation under reduced pressure; mixing the residue with water; extracted the residue with a water-immiscible solvent, such as ethyl acetate; drying the extract over, for example, anhydrous sodium sulfate; and freeing the product from the solvent by distillation. The resulting product can, if necessary, be purified by conventional means, for example, by recrystallization, or the various chromatography techniques, notably preparative thin layer chromatography or column chromatography.

Step A2 may comprise any one or (if appropriate) more of the following reactions:

(i) removing the carboxy-protecting groups either selectively or non-selectively from the group of formula —$COOR^{5a}$ and/or the group R^{7a}, to convert it or them to a free carboxy group as represented by R^5 R^7;

(ii) esterifying any such free carboxy group to provide an ester of the group, for example as illustrated above in relation to R^5;

(iii) converting such a free carboxy group represented by R^5 to a group of formula —$CONR^8R^9$;

(iv) removing the tetrazolyl-protecting group;

(v) converting a cyano group represented by R^{7a} to a tetrazolyl group;

(vi) converting a monoalkylcarbamoyl group or a carbamoyl group represented by R^{7a} first to a cyano group and then to a tetrazolyl group;

(vii) where R^4 represents a tri-substituted silyl group, an aralkyl group, an aliphatic acyl group, an alkoxymethyl group, an alkoxyalkoxymethyl group, a haloalkoxymethyl group, a tetrahydropyranyl group, a tetrahydrothiopyranyl group, a tetrahydrothienyl group, a tetrahydrofuryl group or a substituted tetrahydropyranyl, tetrahydrothiopyranyl, tetrahydrothienyl or tetrahydrofuryl group having a halogen or alkoxy substituent, all of which can be regarded as hydroxy-protecting groups, removing the protecting group to produce a compound in which R^4 represents a hydrogen atom; and

(viii) where R^4 represents a hydroxy group, alkylating or acylating this group.

(i) Removal of carboxy-protecting groups:

The nature of the reaction employed to remove the carboxy-protecting group will, of course, depend on the nature of the group to be removed and are well known in the field of organic synthesis.

For example, where the carboxy-protecting group is an aralkyl group, for example a benzyl or p-nitrobenzyl group, the protecting group may be removed by catalytic reduction, in the presence of hydrogen, which may be under atmospheric pressure or superatmospheric pressure, for example up to 5 atmospheres pressure. The reaction normally and preferably takes place in an inert solvent (preferably an alcohol, such as methanol or ethanol, or a carboxylic acid, such as acetic acid) and in the presence of a catalyst. Any catalyst commonly used for catalytic hydrogenation or reduction may equally be employed here, preferably palladium-on-charcoal or platinum oxide.

Where the carboxy-protecting group is a t-butyl or diphenylmethyl group, it may be removed by reacting the protected compound with an acid (preferably a mineral acid, such as hydrogen chloride or sulfuric acid, or an organic acid, such as trifluoroacetic acid, methanesulfonic acid or p-toluenesulfonic acid) in an inert solvent (preferably an alcohol, such as methanol or ethanol; an ether, such as tetrahydrofuran or dioxane; water; or a mixture of water and one or more of the above organic solvents).

Where the carboxy-protecting group is a silyl group, this may be a group of formula —$SiR^aR^bR^c$, in which R^a, R^b and R^c are as defined above. In this case, the protecting group may be removed by reacting the protected compound with an acid (preferably a mineral acid, such as hydrogen chloride, or an organic acid, such as acetic acid, trifluoroacetic acid, methanesulfonic acid or p-toluenesulfonic acid) or with a fluorine salt, such as tetrabutylammonium fluoride. The reaction normally and preferably takes place in an inert solvent (preferably an ether, such as tetrahydrofuran or dioxane; an alcohol, such as methanol or ethanol; an amide, such as N,N-dimethylformamide or N,N-dimethylacetamide; water; or a mixture of water and one or more of the above organic solvents).

Where the carboxy-protecting group is an ester residue, the protecting group may be removed by hydrolysis using a base (preferably an alkali metal hydroxide, such as lithium hydroxide, sodium hydroxide or potassium hydroxide, or an alkali metal carbonate, such as sodium carbonate or potassium carbonate) in an inert solvent (preferably an alcohol, such as methanol or ethanol; an ether, such as tetrahydrofuran or dioxane; water; or a mixture of water and one or more of the above organic solvents). Where R^4 represents an acyl group, it is removed simultaneously in the course of this reaction.

The reaction can take place over a wide range of temperatures, and the precise reaction temperature is not critical to the invention. In general, we find it convenient to carry out the reaction at a temperature of from 0° C. to 100° C., more preferably from about room temperature to 60° C. The time required for the reaction may also vary widely, depending on many factors, notably the reaction temperature and the nature of the reagents and solvent employed. However, provided that the reaction is effected under the preferred conditions outlined above, a period of from 30 minutes to 24 hours, more preferably from 1 to 16 hours, will usually suffice.

After completion of the reaction, the desired compound may be recovered by conventional means, the nature of which will depend on the nature of the reaction. For example, where the deprotection is carried out by catalytic reduction, the desired product can be recovered by filtering off the catalyst and by distilling off the solvent. Where the deprotection is carried out using an acid, the desired product can be recovered by collecting the precipitate in the reaction system by filtration or by concentration of the reaction mixture. Where the deprotection is carried out by alkaline hydrolysis, the desired product can be recovered by distilling off the solvent and then neutralizing the residue with an aqueous acid, after which the precipitate in the aqueous solvent may be collected by filtration; alternatively, it may be recovered by neutralizing the aqueous layer obtained by extracting the reaction mixture with a water-immiscible organic solvent (such as ethyl acetate or diethyl ether), extracting the neutralized solution with a water-immiscible organic solvent (such as ethyl acetate), and then distilling off the solvent. The reaction product may, if necessary, be further purified by conventional means, for example by recrystallization or the various chromatography techniques, notably preparative thin layer chromatography or column chromatography.

Each of the protecting groups represented by R^{5a} and R^{7a} can be selectively eliminated by appropriate choice of the protecting groups and the specific reaction conditions employed to remove them.

(ii) Esterification

Where a compound containing one or more free carboxy groups is produced, this group or these groups may be

esterified, by methods well known in organic chemistry. For example, the reaction may be carried out by reacting the corresponding carboxylic acid with a compound of formula, R^{5b}-Y [in which R^{5b} may represent any of the groups defined above for R^{5a} other than a hydrogen atom, and Y represents a halogen atom, such as a chlorine, bromine or iodine atom, a group of formula —OSO_3R^{5b}(in which R^{5b} is as defined above) or a sulfonyloxy group, such as a methanesulfonyloxy or p-toluenesulfonyloxy group]. The reaction is carried out in the presence of a base, for example: an organic amine, such as triethylamine, pyridine or N-methylmorpholine; an alkali metal carbonate, such as sodium carbonate or potassium carbonate; or an alkali metal hydrogencarbonate, such as sodium hydrogencarbonate or potassium hydrogencarbonate. It is also normally and preferably carried out in an inert solvent (preferably an amide, such as N,N-dimethylformamide or N,N-dimethylacetamide; a halogenated hydrocarbon, preferably a halogenated aliphatic hydrocarbon, such as methylene chloride; a ketone, such as acetone or methyl ethyl ketone; or an ether, such as tetrahydrofuran or dioxane). Where the desired ester group is an alkyl group, the reaction is carried out by reacting the carboxylic acid with the corresponding dialkyl sulfate.

The reaction can take place over a wide range of temperatures, and the precise reaction temperature is not critical to the invention. In general, we find it convenient to carry out the reaction at a temperature of from 0° C. to 120° C., more preferably from 20° C. to 80° C. The time required for the reaction may also vary widely, depending on many factors, notably the reaction temperature and the nature of the reagents and solvent employed. However, provided that the reaction is effected under the preferred conditions outlined above, a period of from 30 minutes to 24 hours, more preferably from 1 to 16 hours, will usually suffice.

Where a carboxy-protecting group is a C_1–C_6 alkyl group, the esterification reaction may be carried out by reacting the corresponding carboxylic acid with a C_1–C_6 alcohol, such as methanol, ethanol, propanol or hexanol, in the presence of an acid catalyst, such as hydrogen chloride or sulfuric acid, in an inert solvent (for example: one of the C_1–C_6 alcohols which may be used as the starting material described above; a halogenated hydrocarbon, such as methylene chloride; or an ether, such as tetrahydrofuran or dioxane) at a temperature of from 0° C. to 100° C. for a period of from 1 to 24 hours, or by reacting the corresponding carboxylic acid with a halogenating agent (e.g. phosphorus pentachloride, thionyl chloride or oxalyl chloride) in an inert solvent (for example: a halogenated hydrocarbon, such as methylene chloride; an ether, such as tetrahydrofuran or dioxane; or an aromatic hydrocarbon, such as benzene or toluene) at a temperature of about room temperature for a period of from 30 minutes to 5 hours to yield the corresponding acyl halide, which is then reacted with the corresponding alcohol in an inert solvent (e.g. benzene or methylene chloride) in the presence of a base (for example triethylamine; in case of the t-butyl ester, potassium t-butoxide is used as the preferred base) at a temperature of about room temperature for a period of from 30 minutes to 10 hours. The desired compound can be recovered by conventional means, for example, by a similar method to that described in Step A1.

(iii) Formation of a carbamoyl group

Conversion of a carboxy group represented by R^5 to a group of formula —$CONR^8R^9$, in which R^8 and R^9 are as defined above, may be carried out using well known methods, for example by reacting the carboxylic acid compound, in which the group R^7 is protected, with a compound of formula (VI):

R^8R^9NH (VI)

wherein R^8 and R^9 are as defined above).

This reaction consists of the formation of a peptide bond and is generally well known in organic synthetic chemistry. It may be carried out in an inert solvent (preferably a halogenated hydrocarbon, more preferably a halogenated aliphatic hydrocarbon, such as methylene chloride or chloroform; an ester, such as ethyl acetate; an ether, such as tetrahydrofuran or dioxane; or an amide, such as N,N-dimethylacetamide or N,N-dimethylformamide) in the presence of a condensing agent.

Examples of condensing agents which may be used in this reaction include: carbodiimides, such as N,N-dicyclohexylcarbodiimide or 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride; phosphoryl compounds, such as diphenylphosphoryl azide or diethylphosphoryl cyanide; carbonyldiimidazole; and triphenylphosphine-diethyl azodicarboxylate. Of these, we prefer the carbodiimides and diphenylphosphoryl azide. Where a phosphoryl compound is used, the reaction is preferably carried out in the presence of a tertiary amine, such as triethylamine or N-methylmorpholine.

Alternatively, the reaction in this step can be accomplished by reacting the carboxylic acid with a lower alkyl chloroformate, such as ethyl chloroformate or isobutyl chloroformate, in the presence of a tertiary amine, such as triethylamine or N-methylmorpholine, to produce a mixed acid anhydride, or by reacting the carboxylic acid with N-hydroxysuccinimide, N-hydroxybenzotriazole or p-nitrophenol or the like in the presence of a carbodiimide, such as N,N-dicyclohexylcarbodiimide, to produce the corresponding active ester, and subsequently reacting the mixed acid anhydride or the active ester with the amine compound of formula (VI).

As a further alternative, the reaction in this step can be carried out by reacting the carboxylic acid with a halogenating agent, such as phosphorus pentachloride, oxalyl chloride or thionyl chloride, in an inert solvent (for example: a halogenated hydrocarbon, such as methylene chloride; an ether, such as tetrahydrofuran or dioxane; or an aromatic hydrocarbon, such as benzene or toluene) to give the corresponding acyl halide, and then reacting the acyl halide with the amine compound of formula (VI).

All of these reactions can take place over a wide range of temperatures, and the precise reaction temperature is not critical to the invention. In general, we find it convenient to carry out the reaction at a temperature of from −20° C. to 100° C., more preferably from −5° C. to 50° C. The time required for the reaction may also vary widely, depending on many factors, notably the reaction temperature and the nature of the reagents and solvent employed. However, provided that the reaction is effected under the preferred conditions outlined above, a period of from 30 minutes to 24 hours, more preferably from 1 to 16 hours, will usually suffice.

After completion of the reaction, the reaction product can be recovered from the reaction mixture by conventional means. For example, insoluble materials in the reaction system are filtered off; a water-immiscible organic solvent, such as ethyl acetate, and water are added to the filtrate; the organic solvent layer is separated and dried over a drying agent, such as anhydrous magnesium sulfate; and then the solvent is distilled off to leave the desired product. The reaction product may, if necessary, be further purified by conventional means, for example by recrystallization or the various chromatography techniques, notably preparative thin layer chromatography or column chromatography.

(iv) Removal of tetrazolyl-protecting groups

This may be accomplished by reacting the protected compound with an acid. The reaction is normally and preferably effected in an inert solvent.

The reaction is normally and preferably effected in the presence of a solvent. There is no particular restriction on the nature of the solvent to be employed, provided that it has no adverse effect on the reaction or on the reagents involved and that it can dissolve the reagents, at least to some extent. Examples of suitable solvents include: water; an organic acid, such as acetic acid; an ether, such as tetrahydrofuran or dioxane; an alcohol, such as methanol, ethanol or t-butanol; a ketone, such as acetone or methyl ethyl ketone; or a mixture of any two or more of these solvents. Of these, we prefer water, an organic acid, an alcohol or a mixture thereof.

There is no particular limitation upon the nature of the acid used in the reaction, provided that it can normally function as a Bronsted acid. Preferred examples of such acids include: organic acids, such as acetic acid, formic acid, oxalic acid, methanesulfonic acid, p-toluenesulfonic acid or trifluoroacetic acid; and inorganic acids, such as hydrochloric acid, hydrobromic acid, sulfuric acid or phosphoric acid. Of these, we prefer acetic acid, formic acid, trifluoroacetic acid or hydrochloric acid.

The reaction can take place over a wide range of temperatures, and the precise reaction temperature is not critical to the invention. In general, we find it convenient to carry out the reaction at a temperature of from −10° C. to 120° C., more preferably from 0° C. to 100° C. The time required for the reaction may also vary widely, depending on many factors, notably the reaction temperature and the nature of the reagents and solvent employed. However, provided that the reaction is effected under the preferred conditions outlined above, a period of from 0.5 to 24 hours, more preferably from 1 to 16 hours, will usually suffice.

After completion of the reaction, the desired product of this reaction can be recovered from the reaction mixture by conventional means. For example, after distilling off the solvent, the residue is dissolved in water and a water-immiscible organic solvent. The organic layer containing the desired compound is separated and dried over anhydrous magnesium sulfate. After distilling off the solvent, the desired compound can be obtained. The reaction product may, if necessary, be further purified by conventional means, for example by recrystallization or the various chromatography techniques, notably preparative thin layer chromatography or column chromatography.

(v) Conversion of a cyano group to a tetrazolyl group

In this step, a cyano group is converted to a tetrazolyl group by reacting the cyano compound with an alkali metal azide.

The reaction is normally and preferably effected in the presence of a solvent. There is no particular restriction on the nature of the solvent to be employed, provided that it has no adverse effect on the reaction or on the reagents involved and that it can dissolve the reagents, at least to some extent. Examples of suitable solvents include: amides, such as N,N-dimethylformamide or N,N-dimethylacetamide; ethers, such as dioxane or 1,2-dimethoxyethane; and sulfoxides, such as dimethyl sulfoxide.

Examples of suitable alkali metal azides include lithium azide, sodium azide and potassium azide, of which sodium azide is preferred. There is no particular restriction on the amount of alkali metal azide employed, but we generally prefer to use from 1 to 5 equivalents, more preferably from 1 to 3 equivalents, of the alkali metal azide per equivalent of the cyano compound.

We also prefer to carry out the reaction in the presence of an ammonium halide, for example ammonium fluoride, ammonium chloride or ammonium bromide, of which ammonium chloride is preferred. There is no particular restriction on the amount of ammonium halide employed, but we generally prefer to use from 0.5 to 2 equivalents, more preferably from 1 to 1.2 equivalents, of the ammonium halide per equivalent of the cyano compound.

The reaction can take place over a wide range of temperatures, and the precise reaction temperature is not critical to the invention. In general, we find it convenient to carry out the reaction at a temperature of from 70° to 150° C., more preferably from 80° to 120° C. The time required for the reaction may also vary widely, depending on many factors, notably the reaction temperature and the nature of the reagents and solvent employed. However, provided that the reaction is effected under the preferred conditions outlined above, a period of from 10 hours to 7 days, more preferably from 1 to 5 days, will usually suffice.

Alternatively, the cyano group may be converted to a tetrazolyl group by reacting the cyano compound with a trialkyltin azide or triaryltin azide, and then treating the resulting tin compound with an acid, a base or an alkali metal fluoride.

The reaction of the cyano compound with the trialkyltin azide or triaryltin azide is normally and preferably effected in the presence of a solvent. There is no particular restriction on the nature of the solvent to be employed, provided that it has no adverse effect on the reaction or on the reagents involved and that it can dissolve the reagents, at least to some extent. Examples of suitable solvents include: hydrocarbons, which may be aliphatic or aromatic hydrocarbons, such as benzene, toluene, xylene or heptane; halogenated hydrocarbons, especially halogenated aliphatic hydrocarbons, such as 1,2-dichloroethane or chloroform; ethers, such as dioxane or 1,2-dimethoxyethane; amides, such as N,N-dimethylformamide or N,N-dimethylacetamide; and esters, such as ethyl acetate or butyl acetate.

Although there is no particular limitation on the nature of the trialkyltin or triaryl tin azide, and any such compound commonly used in reactions of this type may equally be employed here, we generally prefer to use: a trialkyltin azide in which each of the alkyl groups (which may be the same or different, although they are preferably the same) have from 1 to 4 carbon atoms, for example trimethyltin azide, triethyltin azide or tributyltin azide; or a triaryltin azide in which each of the aryl groups (which may be the same or different, although they are preferably the same) is as defined above in relation to the aryl groups which may be represented by R^2, preferably a phenyl or substituted phenyl group, for example triphenyltin azide or tritolyltin azide. The amount of the trialkyltin azide or triaryltin azide employed is not critical, although an amount of from 1 to 3 equivalents per equivalent of cyano compound is preferred, and from 1 to 2 equivalents is more preferred.

The reaction of the cyano compound with the trialkyltin azide or triaryltin azide can take place over a wide range of temperatures, and the precise reaction temperature is not critical to the invention. In general, we find it convenient to carry out the reaction at a temperature of from 60° to 150° C., more preferably from 80° to 120° C. The time required for the reaction may also vary widely, depending on many factors, notably the reaction temperature and the nature of the reagents and solvent employed. However, provided that the reaction is effected under the preferred conditions outlined above, a period of from 8 hours to 7 days, more preferably from 1 to 5 days, will usually suffice.

The tin-containing compound produced by this reaction is then treated with an acid, a base or an alkali metal fluoride, to convert it to the desired tetrazolyl compound. Any acid, base or alkali metal fluoride commonly used for this type of reaction may be used, and examples of suitable compounds include: acids, especially mineral acids, such as hydrochloric acid or sulfuric acid; bases, especially inorganic bases, such as alkali metal carbonates and hydrogencarbonates (for example sodium carbonate, potassium carbonate, sodium hydrogencarbonate or potassium hydrogencarbonate) or alkali metal hydroxides (for example sodium hydroxide or potassium hydroxide); and alkali metal fluorides, such as lithium fluoride, sodium fluoride or potassium fluoride.

The reaction is normally and preferably effected in the presence of a solvent. There is no particular restriction on the nature of the solvent to be employed, provided that it has no adverse effect on the reaction or on the reagents involved and that it can dissolve the reagents, at least to some extent. Examples of suitable solvents include those listed above for the reaction of the cyano compound with the trialkyltin azide or triaryltin azide and other solvents, such as alcohols (for example methanol or ethanol), water or aqueous alcohols. The reaction can take place over a wide range of temperatures, and the precise reaction temperature is not critical to the invention. In general, we find it convenient to carry out the reaction at a temperature of from 0° C. to 100° C., preferably about room temperature. The time required for the reaction may also vary widely, depending on many factors, notably the reaction temperature and the nature of the reagents and solvent employed. However, provided that the reaction is effected under the preferred conditions outlined above, a period of from 30 minutes to 3 days, more preferably from 1 hour to 24 hours, will usually suffice.

A further alternative method of converting a cyano group to a tetrazolyl group is to react the cyano compound with a trialkyltin halide or triaryltin halide, in the presence of an alkali metal azide, and then treating the resulting tin compound with an acid, a base or an alkali metal fluoride.

The reaction of the cyano compound with the trialkyltin halide or triaryltin halide in the presence of an alkali metal azide is normally and preferably effected in the presence of a solvent. There is no particular restriction on the nature of the solvent to be employed, provided that it has no adverse effect on the reaction or on the reagents involved and that it can dissolve the reagents, at least to some extent. Examples of suitable solvents include: hydrocarbons, which may be aliphatic or aromatic hydrocarbons, such as benzene, toluene, xylene or heptane; halogenated hydrocarbons, especially halogenated aliphatic hydrocarbons, such as 1,2-dichloroethane or chloroform; ethers, such as dioxane or 1,2-dimethoxyethane; ketones, such as acetone or methyl ethyl ketone; amides, such as N,N-dimethylformamide or N,N-dimethylacetamide; and esters, such as ethyl acetate or butyl acetate.

Although there is no particular limitation on the nature of the trialkyltin or triaryl tin halide, and any such compound commonly used in reactions of this type may equally be employed here, we generally prefer to use: a trialkyltin halide in which each of the alkyl groups (which may be the same or different, although they are preferably the same) have from 1 to 4 carbon atoms, for example trimethyltin chloride, trimethyltin bromide, triethyltin chloride or tributyltin chloride; or a triaryltin halide in which each of the aryl groups (which may be the same or different, although they are preferably the same) is as defined above in relation to the aryl groups which may be represented by R^2, preferably a phenyl or substituted phenyl group, for example triphenyltin

chloride or tritolyltin chloride. The amount of the trialkyltin halide or triaryltin halide employed is not critical, although an amount of from 1 to 3 equivalents per equivalent of cyano compound is preferred, and from 1 to 2 equivalents is more preferred.

There is no particular restriction on the alkali metal azide which is also employed in this reaction. Examples include lithium azide, sodium azide and potassium azide, of which sodium azide is preferred. The amount of the alkali metal azide employed is not critical, although an amount of from 1 to 3 equivalents per equivalent of cyano compound is preferred, and from 1 to 2 equivalents is more preferred.

The reaction of the cyano compound with the trialkyltin halide or triaryltin halide in the presence of an alkali metal azide can take place over a wide range of temperatures, and the precise reaction temperature is not critical to the invention. In general, we find it convenient to carry out the reaction at a temperature of from 60° to 150° C., more preferably from 80° to 120° C. The time required for the reaction may also vary widely, depending on many factors, notably the reaction temperature and the nature of the reagents and solvent employed. However, provided that the reaction is effected under the preferred conditions outlined above, a period of from 8 hours to 7 days, more preferably from 1 to 5 days, will usually suffice.

The tin-containing compound produced by this reaction is then treated with an acid, a base or an alkali metal fluoride, to convert it to the desired tetrazolyl compound. The reaction is essentially the same as the reaction of the tin-containing compound (produced by reacting the cyano compound with a trialkyltin azide or triaryltin azide) with an acid, a base or an alkali metal fluoride, and may be carried out using the same solvents and reaction conditions.

(vi) Conversion of an alkylcarbamoyl group or a carbamoyl group to a cyano group

To convert an alkylcarbamoyl group to a cyano group, the alkylcarbamoyl compound is reacted with a halogen compound capable of acting as a halogenating agent, preferably chlorinating agent, for example oxalyl chloride, phosphorus oxychloride or sulfonyl chloride. There is no particular restriction on the amount of halogen compound employed, although we generally find it convenient to use from 1 to 3 equivalents, more preferably from 1 to 2 equivalents, per equivalent of the carbamoyl compound.

The reaction is normally and preferably effected in the presence of a solvent. There is no particular restriction on the nature of the solvent to be employed, provided that it has no adverse effect on the reaction or on the reagents involved and that it can dissolve the reagents, at least to some extent. Examples of suitable solvents include: hydrocarbons, which may be aliphatic or aromatic hydrocarbons, such as benzene, toluene, xylene or heptane; halogenated hydrocarbons, especially halogenated aliphatic hydrocarbons, such as methylene chloride or chloroform; ethers, such as dioxane, tetrahydrofuran or diethyl ether; and esters, such as ethyl acetate or butyl acetate.

The reaction can take place over a wide range of temperatures, and the precise reaction temperature is not critical to the invention. In general, we find it convenient to carry out the reaction at a temperature of from −10° to 100° C., more preferably from 0° to 50° C. The time required for the reaction may also vary widely, depending on many factors, notably the reaction temperature and the nature of the reagents and solvent employed. However, provided that the reaction is effected under the preferred conditions outlined above, a period of from 10 minutes to 16 hours, more preferably from 30 minutes to 6 hours, will usually suffice.

To convert a carbamoyl group to a cyano group, the carbamoyl compound is reacted with a dehydrating agent, for example acetic anhydride, trifluoroacetic anhydride, methanesulfonic anhydride, trifluoromethanesulfonic anhydride, oxalyl chloride or sulfonyl chloride, in the presence of an organic amine, for example triethylamine, pyridine or N-methylmorpholine.

The reaction is normally and preferably effected in the presence of a solvent. There is no particular restriction on the nature of the solvent to be employed, provided that it has no adverse effect on the reaction or on the reagents involved and that it can dissolve the reagents, at least to some extent. Examples of suitable solvents include: hydrocarbons, which may be aliphatic or aromatic hydrocarbons, such as benzene, toluene, xylene or heptane; halogenated hydrocarbons, especially halogenated aliphatic hydrocarbons, such as methylene chloride or chloroform; ethers, such as dioxane, tetrahydrofuran or diethyl ether; and esters, such as ethyl acetate or butyl acetate.

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The desired product of these reactions can be recovered from the reaction mixture by conventional means, for example by neutralizing the mixture with a weak base, such as sodium hydrogencarbonate and then working up the product in a similar manner to that described in Step A1 of Reaction Scheme A.

The cyano compound thus obtained may then be converted to the corresponding tetrazolyl compound, using any of the reactions described above.

(vii) Removing hydroxy-protecting groups

Where R^4 represents a tri-substituted silyl group, an aralkyl group, an acyl group, alkoxymethyl groups, a tetrahydropyranyl group, a tetrahydrothiopyranyl group, a tetrahydrothienyl group, a tetrahydrofuryl group or a substituted tetrahydropyranyl, tetrahydro- thiopyranyl, tetrahydrothienyl or tetrahydrofuryl group, all of which can be regarded as hydroxy-protecting groups, the protecting group is removed, to produce a compound in which R^4 represents a hydrogen atom. The nature of the reaction employed to remove the protecting group, will, of course, depend on the nature of the protecting group, as is well known in the art, and any of the many well known reactions used for deprotecting compounds of this type may equally be used here.

Where the hydroxy-protecting group is a silyl group, it can normally be removed by treating the protected compound with a compound capable of forming a fluorine anion, such as tetrabutylammonium fluoride. The reaction is normally and preferably effected in the presence of a solvent. There is no particular restriction on the nature of the solvent to be employed, provided that it has no adverse effect on the reaction or on the reagents involved and that it can dissolve the reagents, at least to some extent. Examples of suitable solvents include ethers, such as tetrahydrofuran or dioxane.

The reaction can take place over a wide range of temperatures, and the precise reaction temperature is not critical to the invention. In general, we find it convenient to carry